THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 169, NO. 11 — CHICAGO, ILLINOIS — MARCH 14, 1959

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LIFE-TABLE ANALYSIS OF SURVIVAL AFTER CEREBRAL THROMBOSIS—TEN-YEAR EXPERIENCE

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Factors of possible prognostic value have been sought in the records of 1,018 patients with cerebral thrombosis admitted to three major hospitals of Worcester during the years 1947 through 1956. The initial attack was fatal in 21% of the cases. Of the 737 patients who survived the first episode of thrombosis, 50% died within 4.1 years, while only 18% of a comparable sample of the general population died within that time. The principal cause of subsequent mortality was recurrent vascular disease, which accounted for 85% of all deaths. There were no important differences between those who survived and those who did not survive the first attack in regard to the incidence of coronary disease, diabetes mellitus, and hypertension, but the association of congestive heart failure with cerebral thrombosis was found to carry a poorer immediate prognosis. Additional factors adversely affecting prognosis were severe initial attacks, and early recurrences.

THE INCREASING prevalence of cerebral thrombosis in the United States has created many medical, social and economic problems.[1] General pessimism by many in the medical profession toward patients with this disease has retarded interest in any systematic study of its natural course or therapy to improve the status of patients so afflicted. The present investigation of cerebral thrombosis, with use of life-table analysis, was undertaken to determine the factors influencing survival of patients after an initial episode and to aid in designing experimental therapeutic programs. An adequate study of the life history of patients with this disease requires a highly stable population of adequate size that is traceable to determine survival rates. Worcester, Mass., with a metropolitan population of over 500,000, meets these requirements. It was therefore possible to complete such a study.

Material and Methods

A record review of all patients with a diagnosis of cerebrovascular disease admitted to the Memorial, St. Vincent, and Worcester City hospitals during the years 1947 through 1956 was made. Patients with intracranial and subarachnoid hemorrhage,

From the Research Laboratory and Medical Division, The Memorial Hospital, and medical divisions, St. Vincent and Worcester City hospitals. Read, in part, before the Third World Congress of Cardiology, Brussels, Sept. 17, 1958. Read before the New England Cardiovascular Society, Boston, Jan. 12, 1959.

embolism, and neoplasm were excluded. The clinical criteria used to confirm the diagnosis of cerebral thrombosis were those outlined by the *ad hoc* committee of the National Institute of Neurological Diseases and Blindness, under the chairmanship of Dr. Clark H. Millikan.[2] One thousand eighteen

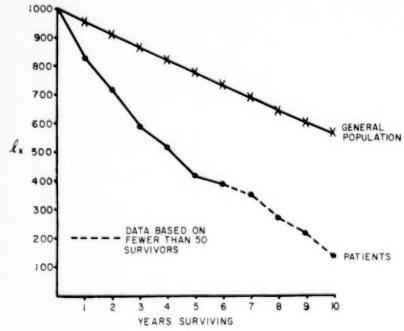

Fig. 1.—Survival of patients with cerebral thrombosis compared to New England population of same age and sex distribution.

records of patients with definite cerebral thrombosis were available for analysis. Of the patients surviving the studied admission, more than 97% were traced by a public health nurse employed by the Research Laboratory. Survival data and appropriate information from the records were transferred to check-cards for sorting. Facts regarding mortality, survival, recurrence, and severity of initial attack were organized in life-table form, as described by Hill.[3] Deaths from all causes were included, and a few patients lost sight of prior to 1957 were included in those exposed to risk for the recorded years only. For comparison, life-tables were constructed based on the New England white population from the United States Census of 1950,[4] adjusted for age and sex. Patients whose initial episodes of cerebral thrombosis occurred prior to 1947 were excluded. The severity of the initial attacks of the remaining survivors was graded as follows: grade 1—few neurological signs and symptoms without residual disability (grade 1A, minimal signs and symptoms, e. g., monoparesis, monoplegia, aphasia, or cranial nerve signs, and, grade 1B, transitory hemiparesis or hemiplegia); grade 2—some neurological signs and symptoms with minimal residuals; grade 3—gross neurological signs and symptoms with disabling residuals; and grade 4—total, permanent incapacitation and/or death due to cerebral thrombosis.

Results

Mortality.—A comparison of the mortality among the survivors of an initial attack of cerebral thrombosis with that expected in the New England white population of similar age and sex is shown in figure 1. The abscissa represents years of survival after the first episode and the ordinate (l_x) the number remaining alive at each year, adjusted to 1,000 initial survivors. During the studied admission 196 patients died, an initial mortality of 21%. The lower curve in the figure was derived from records of 737 patients, the 79% who survived the initial attack. It is clear that, within one year, more than 15% of these survivors had died, in contrast to about 5% in the curve drawn for the hypothetical comparable New England population. Fifty per cent of the patients were dead within 4.1 years, while at the same time only 18% of the general population would have died. The five-year mortality of 59%, in contrast to an expected mortality of 23%, shows that these patients are dying about two and one-half times faster than the general population. Beyond the sixth year the data are unreliable, since the calculations had to be based on fewer than 50 survivors. These results are similar to those recently reported by Pincock,[5] but his survival rates were somewhat higher. As this author points out, however, his results cannot be compared with those of patients from an unselected general hospital population because of the all-male veteran character of his group. Also, there were only 101 survivors avail-

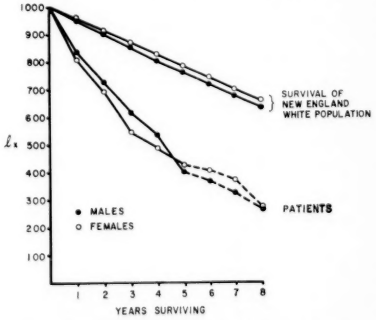

Fig. 2.—Survival of men and women with cerebral thrombosis compared to New England population of same age distribution.

able for his follow-up study. Another recent report by Pierson and Hoobler [6] showed mortalities of 10 to 15% per year, comparable to those of the present study. However, the selection of hypertensive sub-

jects under the age of 50 with a previous episode of "focal encephalopathy" restricted this study to an analysis of 71 patients.

Survival.—The similarity of survival rates in men and women is shown in figure 2. The apparent greater survival at three years of men over women does not reach statistical significance, the probability of chance occurrence (p) being about 0.08 by the chi-square test.[7] The average ages of the men (66.2 years) and women (68.0 years) were similar. Although the increased survival rate of women over men in the New England population does not seem great in this figure, these differences are highly significant because of the large size of the studied population.

Despite the similar survival rates of the men and women, a larger number of women were found in the 196 patients who succumbed during the initial episode of the disease. Indeed, of these patients only 36% were males, representing 17% of all males studied, while the 64% of the 196 who were females

TABLE 1.—*Incidence of Complications in Men and Women Who Died at First Attack Compared to Incidence Among Survivors*

	Died at First Attack		
	Males	Females	All Survivors
Patients, no.	66	116	535
Mean age, yr.	69.6	73.6	68.1
Complication			
Coronary disease, %	29	16	21
Diabetes, %	18	17	13
Hypertension, %	68	69	70
Congestive heart failure, %	32	34	18
None, %	17	10	19

represented 25% of the women in the entire group. In an attempt to determine the reasons for this greater mortality in women, several pertinent complicating factors were studied, as shown in table 1. Since any sex differences in age and complications were found to be insignificant, the explanation for the difference in mortality remains obscure. This table also reveals that survivors of an initial cerebral thrombosis had a much lower incidence of congestive heart failure (18%) than did those who died (33%)—($p<0.001$). Thus, the association of congestive heart failure with cerebral thrombosis carries a poorer immediate prognosis. There were no important differences in the incidence of coronary disease, diabetes mellitus, and hypertension between those succumbing to and those surviving the initial episode.

Of the 737 patients who survived the initial attack, 344 have since died. The causes of death were ascertained from hospital records (some of which included autopsy reports), death certificates, and, in a few instances, interview of relatives. In table 2 are listed both vascular and miscellaneous causes of death in both males and females. As anticipated, recurrent cerebral vascular disease accounted for 53% of all deaths. This is comparable to the 60% reported by Pierson and Hoobler [8] in their series of

TABLE 2.—*Causes of Death in Survivors of First Attack of Cerebral Thrombosis*

	Male (166 Patients)		Female (178 Patients)	
	No.	%	No.	%
Cerebral	87	52	97	54
Coronary heart disease	46	28	53	30
Renal	4	3	2	2
Peripheral vascular disease	1		1	
Total cardiovascular-renal	138	83	153	86
Miscellaneous	28	17	25	14
Bronchopneumonia	14		10	
Cancer	6		7	
Other	8		8	

71 patients. An additional 29% of the deaths in the present series were due to coronary disease, with a total of 85% resulting from all vascular causes.

Recurrence.—In order to study the relationship between early recurrence of cerebral thrombosis and increased mortality, 535 survivors, all those for whom such information was available, were divided into those with recurrence within two years of the initial episode and those without recurrence during this interval. Since at least a two-year follow-up study was necessary, only patients whose first experience occurred between 1947 and 1955 were included. The two groups were similar in size, age, and incidence of complications, as shown in table 3. The higher incidence of congestive heart failure in the early recurrence group was not statistically significant ($0.05<p<0.10$). But life-table analysis of these patients, shown in figure 3, clearly demonstrates that those with early recurrences had a much

TABLE 3.—*Similarity of Incidence of Complications in Patients With and Without Early Recurrence*

	Recurrence		
	Within 2 Yr.	None Within 2 Yr.	All Survivors
Patients, no.	225	310	535
Mean age, yr.	68.8	67.5	68.1
Complication			
Coronary disease, %	22	19	21
Diabetes, %	13	13	13
Hypertension, %	72	69	70
Congestive heart failure, %	22	16	18
None, %	17	20	19

higher mortality, with a 50% survival of only two and one-half years, compared with nearly seven years in the group without early recurrence. Thus, these studies provide statistical evidence for the clinical impression that early recurrence is correlated with poor survival. A more detailed analysis of cumulative recurrences after the initial attack

revealed that over one-third of the patients suffered a recurrence within one year, one-half within two years, and two-thirds by the end of the fourth year.

Severity of Initial Attack.—In order to evaluate the relationship between severity of the initial attack of cerebral thrombosis and mortality, 642 survivors for whom there was sufficient information to grade severity were analyzed by means of life-tables. The tables for grades 2, 3, and 4, all those with residual disability, were combined, since there was no appreciable difference in mortality among them. In figure 4 this combined group is compared with the survivors in grade 1, those without residuals. At three years, the difference in mortality favoring the less severe group (grade 1) was highly significant ($p<0.001$). Since this figure illustrates the difference in mortality between those without and those with residual signs and symptoms, it was of interest to subdivide further the grade-1 group into those with minimal signs and symptoms, grade 1-A, and those with transitory hemiparesis or hemiplegia, grade 1-B. A comparison of the three-year survival rate reveals that group 1-A had only slightly greater mortality than the general population (811 compared with 864 still alive), whereas group 1-B had a mortality nearly comparable to groups 2, 3, and 4 (608 compared with 561 still alive). Thus, despite complete recovery without residual disability, those whose first episodes were more severe and extensive had a much less favorable prognosis than the patients experiencing only mild initial attacks.

Summary

An initial attack of cerebral thrombosis was accompanied by a mortality of 21% in an unselected group of over 1,000 patients admitted to the three major hospitals of Worcester, Mass. Of the 79% surviving the first episode, half had died within 4.1 years, in contrast to an expected mortality of only 18% during this time in the general population, adjusted for age and sex. Although the mortality in women was higher during the initial attack, no sex difference was apparent in long-term survival.

The principal causes of death in patients surviving the initial attack were recurrent cerebrovascular disease and other vascular disorders, accounting for 85% of all deaths. The three factors that adversely affected prognosis were associated congestive heart failure, more severe initial attacks, and early recurrence of the disease.

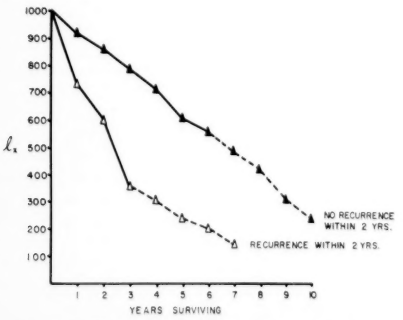

Fig. 3.—Difference in survival of patients with and without early recurrence.

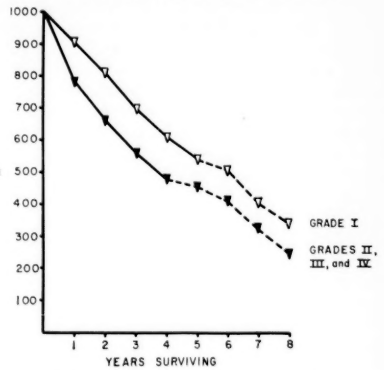

Fig. 4.—Influence of residual disability on survival in cerebral thrombosis.

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This study was supported by a grant from the Albert and Mary Lasker Foundation.

Statistical advice in this study was supplied by Dr. Jane Worcester, Department of Biostatistics, Harvard School of Public Health.

References

1. National Health Education Committee: Facts on the Major Killing and Crippling Diseases in the United States Today, New York, 1957.

2. Classification and Outline of Cerebrovascular Diseases, Report by an ad hoc Committee established by the Advisory Council for the National Institute of Neurological Diseases and Blindness, Public Health Service, Neurology **8:**395-434 (May) 1958.

3. Hill, A. B.: Principles of Medical Statistics, ed. 6, New York, Oxford University Press, 1955, chap. 14.

4. Life Tables for the Geographic Divisions of the United States 1949-51, U. S. Department of Health, Education, and Welfare, Public Health Service, National Office of Vital Statistics, 1956.

5. Pincock, J. G.: Natural History of Cerebral Thrombosis, Ann. Int. Med. **46:**925-930 (May) 1957.

6. Pierson, E. C., and Hoobler, S. W.: Significance of Transient Encephalopathy in Cases of Benign Hypertension, Univ. Michigan M. Bull. **23:**446-455 (Dec.) 1957.

7. Snedecor, G. W.: Statistical Methods, Applied to Experiments in Agriculture and Biology, ed. 5, Ames, Iowa, Iowa State College Press, 1956, chap. 1.

TUBE FEEDING

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Two types of pabulum for administration by nasogastric tube were studied in nine patients who were unable to swallow. Pabulum no. 1 was made from powdered skimmed cow's milk with the addition of cream, glucose, strained liver, and a vitamin concentrate. Pabulum no. 2 was made by a simple formula from one 15.5-(fluid) oz. (458 cc.) can of commercially available soy bean milk diluted with an equal volume of water and supplemented with the same vitamin concentrate. After a week or more on formula no. 1, all patients had diarrhea. After changing to formula no. 2, five became free of diarrhea within 36 hours. Two of the nine patients did not do well on either formula. Analyses of blood, made in all patients at the beginning and end of a two-week period on formula no. 2, showed no indications of biochemical upsets, and there was no clinical evidence of malnutrition. This simple preparation for tube feeding was tolerated by most patients for at least two weeks with a minimum of gastrointestinal and biochemical complications.

In patients to whom intravenously given fluids can no longer supply adequate nutrition, especially calories and amino acids, tube feeding is often used. Material for tube feeding is formulated so as to provide an adequate level of all nutrients within the range of recommended dietary allowances. Aside from supplying adequate nutrition, tube feeding formulas should fulfill the following criteria: (1) be well tolerated and not induce vomiting; (2) be of proper fluid consistency so as to be easily administered and to supply a sufficient water intake; (3) produce a minimum of gastrointestinal complications, such as excessive flatulence, constipation, abdominal distention, and diarrhea; (4) be easily prepared from readily available and reasonably inexpensive materials; and (5) be homogeneous in composition. Palatability of the tube feeding formula, while not of prime importance, is certainly desirable.

The principal tube feeding formula used in the Grace–New Haven Community Hospital is nutritious and generally satisfactory. However, it does require special preparation by the dietetics department, and in a considerable number of patients it produces soft, loose stools and even frank diarrhea. In an attempt to find a tube feeding formula which might produce fewer gastrointestinal complications, such as diarrhea, and be more easily and quickly prepared on the ward, canned soy bean milk [1] was used in 12 selected patients who had first received the usual tube feeding formula no. 1 (analyzed in table 1).

That soy bean milk might be well suited for tube feeding is evident from the ample support in the literature for its use in the management of conditions involving the gastrointestinal tract, such as peptic ulcer, and as a hypoallergenic food for infants, children, and adults. Balfour [2] has noted that foods used in the treatment of upper gastrointestinal irritation should be easy to digest, should contribute little roughage, and are most effective when given in small, frequent feedings. He has observed further that soy bean milk has been noticeably more soothing than ordinary milk to the upper gastrointestinal tract and is seemingly easier to digest. Burke and co-workers [3] found that soy bean milk is as effective as the Sippy milk and cream regimen insofar as influencing the concentration of gastric acidity is concerned.

Glaser, who has studied the problem of allergy in infants, has had wide experience in the use of soy bean milk as a hypoallergenic food. He has reported [4] the successful use of soy bean milk in over 85% of cases in feeding infants from birth and that this may later be substituted by cow's milk formulas without difficulty, except in those infants in whom there is probably a persistent congenital sensitivity to cow's milk.

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Procedure

Nine patients were used in this study, four men and five women, with an over-all age range of 55 to 94 years. Eight of the patients were hospitalized because of severe cerebral vascular accidents, while one patient had postencephalitic paralysis agitans (Parkinson's disease). The latter patient was comatose, was unable to move any extremity, and could not swallow. The other eight patients had hemiplegia and were unable to swallow readily without aspiration. Lumbar punctures were done on all the patients, but only two had red blood cells in the cerebrospinal fluid in sufficient number to indicate bleeding associated with the cerebral vascular accident. None of the patients received anticoagulation therapy. On admission to the hospital, the patients were all given fluids intravenously for periods rang-

ing from three days to one week, and attempts were made routinely to establish whether they could swallow water without aspiration. When it had been established that the patients could not swallow sufficiently well to provide adequate nutrition, the intravenous therapy was discontinued and a nasogastric tube was passed in preparation for tube feeding. Two types of nasogastric tubes were used, i. e., a soft rubber Glenn tube and a small plastic Levin tube. The former tube is preferred because its soft, collapsible, pliable structure minimizes esophageal irritation.

TABLE 1.—*Analysis of Gastrostomy Tube Feeding Formula No. 1**

Ingredients	Amount, Gm.	Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories
Dry skimmed milk powder	100	35.6	1	52	359
Water	750	...	...	...	...
Cream, 20%	150	4.3	30	6	311
Glucose	10	...	...	10	40
Strained liver	30	4.5	1	...	30
Stress formula vitamin concentrate† 1 capsule	...	...	...	...	...
Total		44.4	32	68	740

* Calculated on basis of 1,000 ml., with two-thirds calorie per milliliter.

† One capsule supplies thiamin hydrochloride, 10 mg.; riboflavin, 10 mg.; niacinamide, 100 mg.; ascorbic acid, 300 mg.; pyridoxine hydrochloride, 2 mg.; folic acid, 1.5 mg.; calcium pantothenate, 20 mg.; and vitamin B_{12}, 4 mcg.

After the nasogastric tube was passed, nothing was fed through the tube for the first eight hours, except several 50-cc. volumes of water to insure patency of the tube. For the second eight-hour period, saturated lime water was fed through the tube by giving 25 cc. per hour for the first four hours, then 50 cc. per hour for the second four hours. After this, feeding of the gastrostomy formula no. 1 (table 1) was started, first at the rate of 50 cc. per hour for four feedings and then 100 cc. per hour. Thereafter, in a 24-hour period, a total fluid intake of 2,400 cc. per day was given at the rate of 100 cc. per hour, which supplied 1,776 calories and adequate amounts of protein, fat, carbohydrate, and vitamins, as may be calculated from table 1.

Precautions were taken to have suction readily available at the bedside of these patients in the event of regurgitation or aspiration, and they were given careful nursing supervision. Routine blood testing and urinalyses were done, and nonprotein nitrogen, fasting blood sugar, total serum protein with albumin to globulin ratio, and electrolyte levels were determined at intervals throughout the period of study.

The patients reported here developed frequent loose stools after being on therapy with gastrostomy formula no. 1 for periods ranging from one to two weeks. The development of diarrhea greatly magnifies the nursing problem and enhances the chances of urinary tract infection and the development of decubitus ulcers. After diarrhea had developed, stool cultures were made and, in all cases, grew normal flora. Incidentally, none of these patients were treated with antibiotics during the period of the study. After diarrhea had become a troublesome problem for these patients, they were switched from the therapy with gastrostomy feeding formula no. 1 to that with the soy bean milk preparation.

The soy bean milk [1] used was prepared simply and on the ward merely by dilution of a can of soy bean milk with an equal volume of water. To this were added vitamins in the same amounts used for the gastrostomy formula (table 1). The mixture was stored at the bedside in ice until used. One can of soy bean milk so diluted provides 620 calories.

The feedings of soy bean milk were started at the rate of 50 cc. per hour; after a period of three days this amount was increased so that the patients were receiving, each 24 hours, between 2,400 and 2,790 cc., which provided between 1,600 and 1,860 calories with adequate amounts of protein, fat, and carbohydrate, as may be calculated from table 2.

The patients were continued on therapy with the soy bean milk preparation for a period of two weeks, blood testing done, as indicated above, at the start and end of the two-week period. These results are recorded in table 3.

Results

Of the nine patients switched to the soy bean milk therapy, five responded promptly within 36 hours, with a cessation of diarrhea and the passage of no more than two or three soft, but formed, yellow-brown stools. Two patients continued to have more frequent bowel movements, i. e., five or six per day, of poorly formed stools for the first three or four days on therapy with soy bean milk, after which their stools too were reduced in number to two or three per day.

TABLE 2.—*Composition of Soy Bean Milk (Mull-Soy)*

	Undiluted, %	Diluted with Equal Volume of Water,* %
Water	75.0	87.2
Soy protein	6.0	3.1
Soy fat	7.8	4.0
Carbohydrate	8.9	4.5
Crude fiber	0.3	0.2
Minerals		
Total	2.0	1.0
Calcium	0.26	0.13
Phosphorus	0.22	0.11
Iron	0.0004	0.0002
Calories per fluid ounce	40.0	20.0
Calories per cubic centimeter	1.33	0.66

* 1:1 dilution contains 16 mEq. of sodium per liter.

Two of the nine patients did not respond particularly well either to gastrostomy feeding formula no. 1 or to the soy bean milk. One of these patients occasionally regurgitated the feeding almost as soon as it was given, and great care had to be exercised to avoid aspiration pneumonitis. She also continued to have frequent, loose bowel movements. The other patient had loose, frequent bowel movements

which were not altered by the use of soy bean milk but which were reduced in number by the use of paregoric, 5 cc. given four times a day. No patient given either tube feeding preparations showed distention or constipation or developed other gastrointestinal complications.

As can be seen from table 3, the blood chemistry levels remained stable during the period of feeding of soy bean milk. Further, there was no evidence of unfavorably altered clinical status of these patients during this study.

Comment

Although tube feeding is a life-conserving measure which must often be resorted to in patients who are comatose or who are unable to swallow, every possible effort should be used to attempt to get patients to swallow and take nutrients by the normal mechanism before tube feeding is employed. Tube feeding should be patterned to the need of the patient and not to the convenience of the doctor or nursing staff. The most serious and constant threat in a patient receiving tube feeding is the danger of regurgitation or vomiting, because their inadequate swallowing mechanism practically insures aspiration with its undesirable sequelae unless the patient is immediately given suction or positioned to prevent aspiration. For this reason, suction and close nursing supervision should be available for the tube-fed patient.

The experience reported here indicates that soy bean milk diluted 1:1 with water and supplemented with vitamins is a convenient, relatively inexpensive formula for tube feeding which is well tolerated by the patient and produces a minimum of gastrointestinal complications. It is a physiologically and nutritionally sound preparation which has had long and highly satisfactory usage, especially in pediatric medicine. The fact that its preparation is so simple and can be done on the ward by the nursing staff reduces the work of the usually overtaxed staff of the dietetics department. Further, the amount of the tube feeding preparation made at any one time can be small, thus eliminating spoilage, which may become a vexing problem with the usual specially prepared formulas.

It should be pointed out that, while soy bean milk fortified with vitamins and given as reported above is nutritionally adequate within the range of recommended dietary allowances, it is deficient in iron and, when used for a prolonged period of time, should be supplemented with this element. A most convenient form of iron which has been used for this purpose is iron choline citrate complex, prepared as pediatric drops,[2] which contains 16 mg. of elemental iron per cubic centimeter. Two cubic centimeters of this preparation is added for each can of soy bean milk diluted 1:1 with water.

The low sodium content, i. e., 16 mEq. per liter of the 1:1 dilution, provides an ideal dietary regimen when a low sodium intake is also needed in the management of the patient.

Summary

Nine patients in whom tube feeding had been used and in whom diarrhea became troublesome with the usual skim milk–based formula were given a soy bean milk preparation. This is simply prepared by dilution of a can of the ready-prepared soy bean milk with an equal amount of water and fortification with vitamins. The soy bean milk preparation for tube feeding was effective in returning the bowel movement pattern to normal limits in seven of the nine patients.

333 Cedar St. (11).

The soy bean milk preparation used in this study was supplied as Mull-Soy by the Borden Company, Prescription Products Division, New York. The iron choline citrate complex was supplied as Chél-Iron pediatric drops by Kinney & Company, Inc., Columbus, Ind.

TABLE 3.–*Blood Analyses in Nine Patients with Gastrostomy Feedings*

Case No.	Sex	Age, Yr.	Nonprotein Nitrogen, Mg. %		Fasting Blood Sugar, Mg. %		Total Protein, Gm. %		Albumin, Gm. %		Globulin, Gm. %		Carbon Dioxide, mEq./Liter		Chlorides, mEq./Liter		Sodium mEq./Liter		Potassium, mEq./Liter	
			Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.
1	F	65	42	38	82	86	6.20	6.44	3.21	3.10	2.99	3.34	26.7	28.0	94	93	141	137	5.1	4.8
2	F	55	36	40	91	88	6.73	6.54	3.59	3.60	3.14	2.94	22.7	25.0	96	99	135	140	4.5	4.3
3	M	72	42	39	62	70	8.20	7.82	2.48	2.58	5.72	5.24	30.1	29.0	104	97	144	140	4.1	3.8
4	M	68	51	48	71	80	7.12	7.40	3.00	2.88	4.12	4.52	26.0	29.2	103	100	140	136	4.4	4.8
5	M	71	31	35	68	75	5.82	6.24	2.56	2.40	3.26	3.84	21.0	26.0	92	94	130	134	4.8	4.1
6	F	94	36	41	98	90	6.18	5.88	3.20	3.40	2.98	2.48	28.0	27.1	99	103	140	138	4.4	3.8
7	M	78	48	46	58	79	5.64	5.86	2.34	2.38	3.30	3.48	24.0	22.1	94	98	130	134—	4.6	4.8
8	F	82	59	61	62	68	7.20	7.00	3.10	3.00	4.10	4.00	20.0	19.8	103	106	135	141	4.0	4.4
9	F	62	32	36	71	75	8.02	7.64	3.20	3.62	4.82	4.02	20.0	19.5	104	100	128	134	4.8	4.6

References

1. Manual of Diets, Dietary Department, New Haven, Conn., Grace-New Haven Community Hospital, 1954.
2. Balfour, D. C., Jr.: Control of Stomach Pain, Am. J. Gastroenterol. **22**:181-191 (Sept.) 1954.
3. Burke, J. O.; Regan, W. R.; and Bradford, S.: Study of Concentration of Gastric Acidity in Peptic Ulcer, Internat. Rec. Med. & Gen. Pract. Clin. **167**:586-591 (Nov.) 1954.
4. Glaser, J., and Johnstone, D. E.: Soy Bean Milk as Substitute for Mammalian Milk in Early Infancy, Ann. Allergy **10**:433-439 (July-Aug.) 1952.

INTRAVENOUS UROGRAPHY WITH RENOGRAFIN 60%

A REPORT OF MORE THAN 600 CASES

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The reliability and safety of intravenous urography were studied in 654 patients. The injection consisted of 25 cc. of Renografin (a 60% aqueous solution of the methylglucamine salt of 3,5-diacetylamido-2,4,6-triiodobenzoate) given over a period of three minutes; in only three cases were smaller doses used. There were no severe reactions, but vomiting occurred in 11 patients. One of these had a history of allergy, and another had not been properly prepared. The low incidence of reactions was striking because the ages of the patients ranged from 7 to 84 years and 16 had histories of allergy or severe reactions to previously administered contrast agents. Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure.

In the 30 years since Osborne and co-workers [1] first attempted to visualize the urinary tract in laboratory animals with intravenously given sodium iodide, intravenous urography has become a widely accepted clinical procedure in urologic diagnosis. According to one estimate, a total of 11,546,000 intravenous urographic procedures were performed in the United States alone from 1942 to 1956, the annual number increasing from 280,000 in 1942 to 1,368,000 in 1956.[2] This remarkable progress within a relatively short time—from laboratory experiment to universally employed diagnostic tool—has come about largely because of the successful development and introduction of new and improved contrast agents.

In 1928 Binz and Räth [3] and in 1930 Swick [4] reported the use of uroselectan after the discovery that selectan-neutral provided good contrast of the kidney, but its use was attended by toxic manifestations. In 1929, uroselectan B (Neo-iopax) was introduced, this being less toxic than uroselectan.[5] Several years later, iodopyracet (Per-abrodil [Diodrast]) was developed, and, for 20 years thereafter, iodopyracet and uroselectan B were commonly used in the majority of intravenous urographic procedures in the United States.[2] More recently, a number of new contrast mediums have been introduced in the United States, the most prominent being perhaps Hypaque and Urokon.

In 1955, a new, organic, tri-iodinated radiopaque compound, identified as Renografin, became available for clinical trial in intravenous urography. After preliminary trials of this material in both the 76 and 60% concentrations, results of which have been reported elsewhere,[6] Renografin 60% has been used exclusively at this clinic for intravenous urography in ambulant patients. Individual case reports have been recorded at the time of examination of each patient, with particular attention to signs of sensitivity or other reaction or vessel pain and to the quality of the urograms obtained with this medium. From April, 1957, to the time of this report, over 600 patients were examined with Renografin 60%. Urograms of diagnostic quality have been consistently obtained with practically no side-effects. The purpose of this communication is to describe briefly our experience with Renografin 60% at this large private clinic during the past year and a half.

Methods and Materials

Patients.—A total of 654 patients is included in this report, 394 male and 260 female. They ranged in age from 7 to 84 years and in weight from 50 to 255 lb. (22.7 to 115.6 kg.). Sixteen patients had a history of hay fever, asthma, or severe reaction to previously administered contrast agents. Each of the 654 patients had presented signs or symptoms of disorders related to the urinary tract or renal pelvis and had been referred to the clinic for diagnosis. The distribution of the patients with reference to age, sex, and weight appears in table 1.

Contrast Medium.—Renografin 60% contains 60% of the methylglucamine salt of 3,5-diacetylamido-2,4,6-triiodobenzoate (diatrizoate) in aqueous solution adjusted to neutrality with sodium hydroxide. The solution contains approximately 29.26% iodine.

Method of Study.—Prior to examination, standard instructions for preparation were given to each patient. Each was advised to take 12 fl. oz. (360 cc.) of magnesium citrate solution 36 hours before coming for examination to eat lightly the day before, and, after midnight, to take nothing by mouth except coffee and toast for breakfast. (Eight patients were examined without such preparation.)

In earlier studies with Renografin, a preliminary test dose of 1 cc. was routinely administered to each patient before examination. In the absence of any reaction whatsoever, use of the test dose was finally abandoned. In fact, none was given to any patient in this series.

At examination, 25 cc. of Renografin 60% was given intravenously over a period of three minutes to every patient, with three exceptions. Only 15 cc.

was given to two boys aged 10 and 13 years, respectively, and 10 cc. was given to an adult patient who had had a severe reaction to a previously administered dye and was apprehensive about the possibility of a similar reaction to Renografin—which did not occur. Films were exposed at 5, 10, and 15 minutes after injection, with the patient erect at the final film. The resulting urograms were evaluated and classified as excellent, good, and fair (there were no poor films), mainly on the basis of the presence or absence of a clear-cut pyelogram in good density, regardless of the age, weight, kidney function, or lack of preparation of the patient.

TABLE 1.—*Data from 654 Patients Subjected to Intravenous Urography with Renografin 60%*

	No. of Patients		
Age, Yr.	Male	Female	Total
0-10	5	1	6
11-20	18	8	26
21-30	19	46	65
31-40	38	65	103
41-50	71	42	113
51-60	92	42	134
61-70	84	34	118
>70	67	21	88
Not recorded	0	1	1
Total	394	260	654
Weight, Lb.			
<100	12	12	24
100-110	3	42	45
111-120	7	37	44
121-130	20	30	50
131-140	32	57	89
141-150	57	37	94
151-160	51	13	64
161-170	56	12	68
>170	152	19	171
Not recorded	4	1	5
Total	394	260	654

Results

A summary appears in table 2 of the quality of films obtained with Renografin 60% and the associated reactions encountered. It is evident from this table that good to excellent delineation of the renal collecting system was achieved in 636 of the 654 cases, while only a fair outline was demonstrated in the remaining 18. As anticipated, the greatest proportion of satisfactory films was seen in younger persons of lighter weight. The excretory capacity as a rule is better in younger subjects. Older patients are more difficult to prepare for urographic examination. Moreover, in older persons intestinal gas often obscures and sometimes blocks out kidney delineation even though the dye may be present in the kidney in sufficient concentration to give a good contrast. The quality of films obtained in the individual patients with reference to their respective ages and weights appears in table 3.

TABLE 2.—*Summary of Results in Intravenous Urographic Examination with Renografin 60%*

	Total No. of Patients			No. of patients Showing Reactions		
Quality of Films	Male	Female	Total	Male	Female	Total
Excellent	62	44	106	3	7	10
Good	318	212	530	14	14	28
Fair	14	4	18	2	0	2
Total	394	260	654	19	21	40

TABLE 3.—*Quality of Films Obtained with Renografin 60% with Reference to Age and Weight*

	Quality of Films (No. of Cases)			
Age, Yr.	Excellent	Good	Fair	Total
0-10	6	18	0	6
11-20	7	19	0	26
21-30	23	40	2	65
31-40	28	75	0	103
41-50	21	87	5	113
51-60	15	114	5	134
61-70	8	107	3	118
>70	2	83	3	88
Not recorded	0	1	0	1
Total	106	530	18	654
Weight, Lb.				
<100	6	18	0	24
100-110	10	34	1	45
111-120	11	31	2	44
121-130	6	42	2	50
131-140	10	74	5	89
141-150	11	82	1	94
151-160	9	53	2	64
161-170	11	56	1	68
>170	29	139	3	171
Not recorded	3	1	1	5
Total	106	530	18	654

There were no severe reactions in any patient in the entire series. A total of 40 patients reported 58 different reactions to the dye, but these reactions were relatively mild and transient in every case. Of the 40 patients with reactions 4 had a history of allergy; 2 had not received the standard preparation prescribed before examination. The incidence of reactions encountered in this study is given in table 4.

TABLE 4.—*Incidence of Reactions in Forty Patients Subjected to Intravenous Urography with Renografin 60%*

Reaction	Patients,* No.	History of Allergy, No.	Unprepared for Examination,† No.
Nausea	32	2	2
Vomiting	11	1	1
Choking sensations	2	0	
Flushing of skin	8	0	
Tingling of extremities	2	0	
Itching sensations	1	0	
Urticaria	1	0	
Sneezing	1	1	
Total	58	4	3

*Same patient reported one, two, or even three different reactions in number of instances.

†Same patient reported nausea and vomiting in one instance.

Comment

The relatively few and mild reactions encountered in this series is the most striking feature of this study. It is hard to believe that any drug introduced intravenously could be so well borne by so many patients as has Renografin 60% in this large series. The rate of occurrence of reactions is 6%

(40 of 654 patients), which is in accord with the reaction rate reported by others using this medium.[7] Since films of good or excellent quality were obtained in a high percentage (97%) of the cases examined with Renografin 60%, this contrast agent is obviously satisfactory for use in intravenous urography.

Summary and Conclusions

Intravenous urographic examinations have been conducted in a total of 654 patients with use of Renografin 60% as the contrast agent. Satisfactory films were obtained in 636 (97%) without serious reactions to the medium. Mild reactions, such as nausea, vomiting, a sensation of itching, flushing of the skin, urticaria, sneezing, and a choking sensation, were reported by a total of 40 patients.

On the basis of the high percentage of good or excellent films obtained with Renografin 60% and the remarkably few and mild reactions encountered, it is concluded that Renografin 60% is a superior contrast agent for intravenous urography in the ambulant patient.

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References

1. Osborne, E. D., and others: Roentgenography of Urinary Tract During Excretion of Sodium Iodid, J. A. M. A. **80:**368-373 (Feb. 10) 1923.

2. Pendergrass, H. P., and others: Reactions Associated with Intravenous Urography: Historical and Statistical Review, Radiology **71:**1-12 (July) 1958.

3. Binz, A., and Räth, C.: Über biochemische Eigenschaften von Derivaten des Pyridins und Chinolins, Biochem. Ztschr. **203:**218-222, 1928.

4. Swick, M.: Intravenous Urography by Means of Uroselectan, Am. J. Surg. **8:**405-414 (Feb.) 1930.

5. Maluf, N. S. R.: Role of Roentgenology in Development of Urology, Am. J. Roentgenol. **75:**847-854 (May) 1956.

6. Orr, L. M.; Campbell, J. L; and Thomley, M. W.: Study of Renografin, Monogr. Therap. **1:**12 (Jan.) 1956.

7. Culp, D. A.; Van Epps, E. F.; and Edwards, C. N.: Comparative Studies of Urographic Media, J. Urol. **78:**493-495 (Oct.) 1957.

BRONCHIAL ASTHMA DUE TO FOOD ALLERGY ALONE IN NINETY-FIVE PATIENTS

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Bronchial asthma due to food allergy [1] alone or associated with inhalant allergy is too frequently overlooked. This is due to failure to recognize the typical history of bronchial asthma due to food allergy,[2] especially in children, and its equivalent in adults, including older persons, as summarized below. It also results from the frequency of negative skin reactions to foods causing the asthma [3] and the usual failure of positive skin findings to reveal the responsible foods. Thus, most diets excluding foods giving positive skin reactions fail to control bronchial asthma due to food allergy.[3A] Our realization of the frequency of food allergy therefore has depended on trial diets, of which our cereal-free elimination diet [4] has been most important. Our success has depended on the elimination of all cereal grains, along with milk, egg, chocolate, fish and other less common allergenic foods. Recurrent colds and bronchitis with or without slight wheezing during the fall, winter, and spring months also require similar study of food allergy, as revealed by good results with its use.

The assumption that bronchial asthma is due to inhaled allergens, such as the pollens, has sometimes resulted in overlooking allergens in food. Food allergy has too often been ignored or inadequately controlled when it was the sole cause of bronchial asthma or contributed to the effects of inhaled allergens. Recognition of the importance of food allergy in a given patient is usually impossible unless one begins with a cereal-free elimination diet which assumes allergy to cereal grains as well as to milk, eggs, and other less common allergenic foods. This was clearly demonstrated in 50 children and 45 adults, whose bronchial asthma was relieved without use of antigens, vaccines, corticosteroids, or ACTH. Strict adherence to the diet was necessary at first, especially in the winter, but in many cases it was found that tolerance to some foods developed in one to four years and that a more liberal diet could be allowed in the summer.

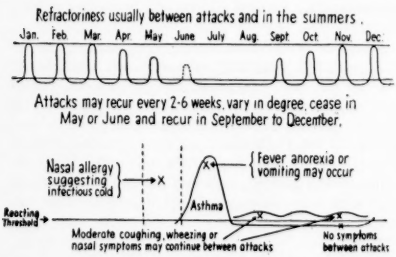
Read in the Session on Allergy before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

Our emphasis on food allergy does not detract from the equally important inhalant allergy [5] alone or in association with food sensitization. The role of pollen allergy in asthma limited to the pollen seasons and the importance of animal emanations, house dusts, miscellaneous inhalants, and fungi must be remembered. Positive skin reactions to inhalants, however, do not predetermine clinical allergy. Assurance of such allergy requires long-lasting relief of asthma with desensitization therapy and/or environmental control. Unnecessary and, at times, prolonged ineffectual desensitization to inhalants too often has preceded the relief of bronchial asthma arising from our cereal-free elimination diet.

This increased recognition of food allergy as the cause of bronchial asthma [1a] has minimized possible bacterial infection or allergy [5A] as the cause, as reported by Cooke,[6] Chobot [7] and other allergists. The occurrence of viral or infectious colds and bronchitis without resultant asthma [1] when it is controlled with elimination of causative foods supports our conclusion that infection is a rare cause of the recurrent bronchial asthma.

Typical History

Recurrent bronchial asthma [8] every two to six weeks, being moderate or severe for one to three days, diminishing in the subsequent one to five days, and decreasing or absent in the summer always suggests food allergy (see figure). It usually starts in the first three years, though a similar or equivalent history occurs in adult life and old age. Initial nasal symptoms suggesting an infectious cold, often with slight fever, generally are wrongly attributed to infection rather than food allergy as the cause. Moderate or severe bronchial asthma then occurs for one to three days with a gradual decrease in one to five days. Fever, due to food allergy, up to 104 F (40 C), is frequent. Anorexia and vomiting may occur. Antibiotics, sulfonamides, and gamma globulin therefore are infrequently justified. Exhaustion of assumed reacting bodies to the allergenic foods terminates the attack. With their regular reaccumulation to the reacting level, attacks recur. Absence of reacting bodies between attacks allows the ingestion of allergenic foods without asthma. If they are not entirely exhausted, slight, interim symptoms may occur. Tolerance for the allergenic foods may develop if the food allergy is controlled for one to four years.



Recurrent attacks of bronchial asthma due to food allergy, especially in children.

Table 1.—*Bronchial Asthma Due to Food Allergy Alone in Infants and Children (Fifty Cases)*[*]

Males, %	66	Symptoms between attacks	
Females, %	34	Nasal, %	58
Age, yr. (av., 5.1)	3/4-13	Bronchial, %	36
Age at onset, yr. (av., 1.6)	1/6-6	Former nasal allergy, %	18
Time with asthma, yr. (av., 3.4)	1/4-9	Former eczema, %	38
Duration of attacks, days	2-10	Former GI symptoms, %	44
Typical history, %	74 / 92	History of possible food allergy, %	50
Less typical history, %	18	Family history of possible allergy, %	80
"Cold" at onset of attack, %	78	Eosinophilia (blood), % (av., 5.4)	0-19
Fever with attacks (under 101 F), %	38 / 60	Skin reactions	
Fever with attacks (101-105 F), %	22	Foods, %	52
Vomiting with attacks, %	36	Pollens,† %	30
Attacks absent in summer, %	44 / 82	Animal emanations,† %	20
Attacks decreased in summer, %	44	Miscellaneous,† %	4
		House dust,† %	26
		Av. time of supervision, yr.	1-8

[*] No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.
†No therapy based on skin reactions.

That infection is not the cause is evidenced by the occurrence of true infectious colds or even pneumonitis with no asthma if the allergenic foods are eliminated. Recurrent colds, with or without coughing and with little or no wheezing, also are often due to food allergy alone rather than infection.

Children.—To emphasize food allergy as a sole cause of bronchial asthma, the statistics in table 1 on 50 infants and children are presented to show bronchial asthma controlled with the elimination of allergenic foods without any injections of inhalant allergens or vaccines and with no corticosteroids, ACTH, antibiotics, or chemotherapy. Many more cases due to food allergy alone are omitted because of brief or longer injections of antigens or vaccines which we now realize were unnecessarily given, largely because of positive skin reactions. A few cases due to food allergy are not included either, because injections of gamma globulin were given and this is of unproved value in asthma.[9] Though antibiotics and chemotherapy are not indicated during attacks of asthma due to food allergy alone, it is justifiable to give such medicaments and respiratory vaccines to help infrequent, secondary infections in such asthma-free persons in all age groups.

The classic or nearly typical history of bronchial asthma due to food allergy is seen to have occurred in 92%. Initial "colds" suggesting infection but due to food allergy occurred in 78%. Antibiotics and sulfonamides had been given ineffectively to some patients for months or years because of assumed infection. Previous fever in 60% and vomiting in 36% did not occur with our control of food allergy. The asthma was decreased or absent in summer in 82%.[10] Slight nasal symptoms in 58% or bronchial symptoms in 36% between previous attacks were relieved with the elimination diet. The former eczema, blood eosinophilia, and recurrent colds were probably results of food allergy. Negative

scratch reactions to foods occurred in 48%. The reactions we obtained gave little or no help in our study of food allergy. The positive reactions to inhalants were either nonspecific or due to potential or past allergy, since the control of food allergy alone gave the desired relief. Diet history of food dislikes or disagreements correlated with the clinical allergies in a few patients, especially in cases of milk and egg sensitization. Family histories of probable allergy at times only in aunts, uncles, or grandparents, usually of asthma or "sinus trouble" occurred in 80%.

Comments from parents reflected the importance of the control of food allergy in bronchial asthma in children and indicated that satisfactory results were obtained with the elimination diet alone.

Adults 15 to 55 Years of Age.—The classic history of bronchial asthma due to food allergy occurs in some adults.[11] Usually the asthma is perennial, decreasing or infrequently absent in the summers. Though interim relief between attacks is less than that in children, careful interrogation usually reveals cyclic exaggeration of the chronic asthma, due, in our opinion, to intermittent activation of the causative food allergy. Fever due to food allergy[12] is infrequent in these adults as compared with children. When present, especially if it is prolonged, infrequent secondary infections also have to be considered. The importance of adequate study of allergy in perennial bronchial asthma usually exaggerated from autumn to spring was dramatized in a young woman with such asthma for several years. Finally it persisted without relief from November to March, when a right lower lobectomy was done for assumed questionable bronchiectasis. Because of postoperative infection, decortication of the right lung was necessary after six weeks. The severe asthma continued for four months until our study indicated probable food allergy. With the cereal-free elimination diet, relief occurred in one month and has continued to the time of writing. Such control of food allergy relieved the patient in another case in which lobectomy also had been advised on the basis of questionable x-ray and bronchoscopic findings. As in children, recurrent head and especially bronchial "colds" particularly from autumn to late spring are often relieved with the routine and accurate use of the cereal-free elimination diet, disproving infection as the cause.

TABLE 2.—*Bronchial Asthma Due to Food Allergy Alone in Thirty Adults 15 to 55 Years of Age**

Male, %	43
Female, %	57
Age, yr. (av., 34.8)	17-53
Age at onset, yr. (av., 20.8)	1/2-47
Duration, yr. (av., 14)	1/2-39
Perennial symptoms, %	100
Recurrent attacks, %	50
Worse in winter, %	47
Absent in summer, %	0
Better in summer, %	40
Better inland, %	10
Other manifestations of allergy	
Nasal allergy, %	80
Nasal polyps, %	10
Eczema, %	10
Hives, %	10
GI symptoms, %	10
Headaches, %	5
History suggestive of	
Food allergy, %	50
Inhalant allergy, %	0
Family history, %	46
Asthma, %	40
Nasal allergy, %	20
Cutaneous allergy, %	3
Headaches and GI symptoms, %	3
Skin reactions (scratch method)	
Foods, %	20
Pollens,† %	50
Animal emanations and miscellaneous,† %	43
House dust,† %	26
Eosinophilia (blood), % (1-22)	9.8
Duration of cooperation, yr. (range 1/2-7)	1.6
Previous corticoids, %	13

* No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.
†No therapy based on skin reactions.

If inhalant allergy, especially pollen, is associated with food allergy, the usual decrease or absence of symptoms in the summer[10] when food is the sole cause may not be observed. Recurrent asthma due to food with more persistent asthma from spring to late fall, moreover, occurs in the same patient.

Statistics on 30 cases of bronchial asthma due to food allergy in adults are given in table 2.

Because of the perennial, usually recurrent, exaggerated asthma, food allergy was studied with our cereal-free elimination diet before any injectants were given. With strict cooperation, relief was evident in one to four weeks. Manipulation of the diet thereafter gradually revealed the foods responsible for the asthma. This stresses the importance of recognizing food allergy and the futility of desensitization and vaccine therapy in such cases. It is rare today, however, that patients with perennial bronchial asthma are not given injectant therapy and that any adequate control of food allergy occurs. In several of these patients, such injections had been given for one to three or more years before our study of food allergy improved or controlled the asthma in one to four weeks.

As in children, skin reactions to foods infrequently correlated with clinical allergies. Moreover, therapy based on the recorded positive reactions to inhalants was not required.

In these adults the average age when first seen was 34.8 years. The age of onset of asthma was 20.8 years. Nasal allergy occurred in 80%. Asthma was worse in the winter in 47%. In the family history, the predominating clinical allergy was bronchial asthma in 40%. Blood eosinophilia occurred in 9.8%.

Adults Over 55 Years of Age.—For many years we have reported bronchial asthma due to food allergy in older patients.[13] Inhalant allergy with or without food allergy has been of similar importance. This refutes opinions of other allergists that inhalant and especially food allergies are rare or even absent, especially after the age of 50 years. In 1947 we reported 173 patients relieved of bronchial asthma who were over 55 years of age.[14] In 82%, food, inhalant, and rare bacterial allergy were causative; 40% were due, in our opinion, to food allergy alone. Thus food and inhalant allergies by our analyses were of equal importance.

In table 3 statistics are presented on 15 patients over 55 years of age with bronchial asthma controlled by the elimination of specific foods alone. This group would have been greater if we, like the majority of physicians, had not given unwarranted injections of inhalants or vaccines because of positive skin reactions or assumed infection. Moreover, cases of asthma exaggerated or occurring only in the

fall, winter, and spring which were controlled with the use of our cereal-free elimination diet but in which pollen therapy was given because of active or potential pollen sensitization from late spring to fall are not included. In the last few years we have refrained from such injectant therapy when food allergy seemed to be the sole cause of the asthma and after it was adequately controlled with the elimination diet alone.

Bronchial asthma in 15 patients over the age of 55 years was controlled only with the elimination of allergenic foods. In spite of slight to moderate reactions to inhalants, no injections of antigens or vaccines were given. Asthma had existed for four months to 54 years with an average of 10 years. The age of onset was from 2 to 57 years with an average age of 30 years. Asthma was perennial except in one case. As in the classic history of asthma due to food allergy in children, the asthma was better in 46% and absent in one case in the summer months. There was no complete interim freedom between attacks, though recurrent exaggeration of asthma was evident in the histories of 40%. Improvement occurred in the summer in 40% and in dry, inland areas in 13%.[10] Nasal allergy had occurred in 66%. Drug allergy, especially to aspirin, occurred in 20%. Corticoids and/or ACTH had been given with no benefit to 20% of these patients before they were relieved with our elimination diets. They were not included in our results. Infective and intrinsic causes had been erroneously assumed in several of these patients.

Thus food and/or inhalant allergies must be studied in all patients with bronchial asthma in old age. Recognition of cardiovascular and renal disease, emphysema, and other causes of wheezing and dyspnea is necessary, of course, especially in this age group. Complete relief of such cases of bronchial asthma or asthmatic bronchitis, exaggerated or only occurring from fall to spring, minimizes possible infective or intrinsic causes. Only death terminates the development or continuance of such allergies in old age.

Study and Control of Food Allergy

Food allergy requires study when the classic history of bronchial asthma due to food allergy in childhood or similar or less typical perennial histories in adults and old age occur. It is also necessary when food and inhalant allergies are indicated causes.

To study and control food allergy, a diet which excludes foods that give large scratch reactions and/or a history of definite food dislikes or disagreements may be effective. The intradermal method of testing is not used in our study because of the many indefinite or false reactions which arise. Relief infrequently results because of the known fallibility of skin testing,[3A] especially in food allergy, and the frequent failure of diet histories to indicate any or all allergenic foods.

The cereal-free elimination diet[4] is then given, with indicated modifications. Indeed, it is usually used without the initial elimination of foods giving positive skin reactions or a positive diet history.

For good results, strict adherence to the diet is imperative, with maintenance of proper weight and nutrition. Realization that foods remain in the body for several days or longer is important. This, together with the time necessary for the disappearance of changes in the lungs, especially in chronic bronchial asthma, explains the time required for control of symptoms. Because of these facts a moderate attack may occur in one to three weeks after the start of the diet free of allergenic foods. The next expected attack, however, should be absent. If food allergy causes persistent or interim symptoms, some relief may not be evident for 5 to 10 days.

Inhalation of odors of allergenic foods must be minimized or avoided. The absence or decrease of symptoms due to food allergy during the summer and the increase in the fall, winter, and early spring

TABLE 3.—*Bronchial Asthma Due to Food Allergy Alone in Fifteen Patients over 55 Years of Age*[*]

Male, %	66	History suggestive of	
Female, %	34	Food allergy (especially	
Age, yr. (av., 60)	55-70	milk), %	66
Age at onset, yr. (av., 30)	2-57	Drug allergy, %	20
Duration, yr. (av. 10)	1/3-54	Inhalant allergy, %	0
Recurrent attacks, %	40	Family history	
Perennial, %	93.4	Bronchial asthma, %	26
Worse from fall to		Nasal allergy, %	13
summer, %	46	GI symptoms, %	13
Absent in summer, %	6.6	Skin reactions	
Better in summer, %	40	Food, %	33
Better inland, %	13	Pollen,† %	40
Other manifestations of allergy		Animal emanations and	
Nasal allergy, %	66	miscellaneous,† %	33-1/3
Polyps, %	13	House dust,† %	20
Hives, %	13	Eosinophilia (blood), %	
		(2-32)	8.3
		Duration of cooperation, yr.	
		(2-2)	1/2-10

[*] No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.
†No therapy based on skin reactions.

months must be remembered.[10] This usually allows a liberal summer diet and requires a strict winter elimination diet to control the food allergy. Injections of inhalants or vaccines should not be given when food allergy is the probable or proved cause. If the cereal-free elimination diet fails to relieve asthma in three to four weeks, however, then such injections are justified if the history with or without positive skin reactions indicates inhalant allergy. Needless injections of inhalants or vaccines are costly and tend to decrease the importance of food allergy and the required elimination diet in the minds of patient and physician alike.

Until relief of symptoms occurs from the elimination of allergenic foods or when symptoms recur from breaks in the diet or trial ingestion of causative foods, severe, at times intractable, asthma from food allergy requires epinephrine given hypodermically, aminophylline by vein or rectum, corticosteroids, ACTH, and adequate replacement of fluid and electrolytes. Less severe attacks or persistent symptoms require epinephrine given subcutaneously

or by inhalation, aminophylline, ephedrine, and, if necessary, corticosteroids. Other inhalant therapy and, at times, antihistamines, isoproterenol (Isuprel), and iodides may be helpful.

The cereal-free elimination diet should be ordered immediately if the history gives any suggestion of food allergy. If nausea is present, parenterally given fluids and the preparation of the diet in a liquid or soft form are indicated until the appetite returns. The immediate use of the diet will hasten the control of food allergy and the discontinuance of the above medication.

As long as symptoms continue to require medication, physicians are challenged with the study and control of possible allergy to other foods, to inhalants, or to rarer infectants and drugs. Errors in the diet must always be suspected. When inhalant, drug, or rare infectant allergies accompany food allergy or are sole causes, their study and control obviously are necessary. The control of bronchial asthma with antiallergic therapy alone without medication is the physician's responsibility.

Summary

Food allergy as the sole cause of bronchial asthma or associated with inhalant or rare infectant or drug allergy is too often ignored and inadequately controlled by the medical profession. The classic history consists of regularly recurring attacks of bronchial asthma, usually preceded by nasal allergy suggesting an infectious cold rather than the causative food allergy. The attacks recurring from fall to late spring are often associated with vomiting and fever due to food allergy. The asthma decreases or is absent in the summer. It usually starts before the third year, though a similar history may begin in adult life or old age. Interim relief between the attacks is usual in childhood, decreasing in adolescence and in adult life.

The use of antibiotics and/or sulfonamides during attacks or daily for months or even years and the recent injections of gamma globulin for wrongly assumed infective asthma are unnecessary, costly, and of potential danger. Continued or intermittent corticosteroid therapy is unnecessary when food allergies are controlled.

In 50 children, 30 adults, and 15 older persons, relief was achieved without use of antigens, vaccines, corticosteroids, or ACTH. A larger number of such cases could have been reported had we not been tempted to inject inhalants and vaccines needlessly in cases we now realize were due to food allergy alone. Food allergy associated with inhalant allergy as a minor or major cause is also too often unrecognized. Bronchial asthma due to inhalants alone is frequent.

Recognition of the classic history of bronchial asthma due to food allergy and its control in children, adults, and in older persons has depended on our initial use of the cereal-free elimination diet which assumes allergy to cereal grains, as well as to milk, egg, and other less common allergenic foods. Strict adherence to this diet and maintenance of protein requirements and weight are necessary. The decrease or entire suppression of food allergy in the summer with exaggeration in the fall, winter, and early spring frequently allows a liberal diet in the summer compared with a strict elimination diet in the winter. Tolerance for foods may arise in one to four years, or such a diet in the winter may be required for many years.

The control of bronchial asthma with corticosteroids, ACTH, and other new and old drugs without the adequate and persistent study of allergenic causes and especially of the usually neglected food allergy is unscientific. It unfortunately ignores the responsibility of the profession to recognize and control atopic allergy which is causative in practically every patient.

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References

1. Rowe, A. H., and Rowe, A., Jr.: (*a*) Bronchial Asthma in Infants and Children: Its Diagnosis and Treatment, California Med. **69:**261-268 (Oct.) 1948. (*b*) Bronchial Asthma in Adults: Causes and Treatment, ibid. **72:**228-233 (April) 1950. (*c*) Bronchial Asthma in Patients over Age of 55 Years: Diagnosis and Treatment, Ann. Allergy **5:**509-518 (Nov.-Dec.) 1947.

2. Rowe, A. H.: Food Allergy: Reasons for Delayed Recognition and Control by Physicians, Quart. Rev. Allergy **8:**391-403 (Sept.) 1954.

3. Rowe, A. H.: Evaluation of Skin Reactions in Food Sensitive Patients, J. Allergy **5:**135-147 (Jan.) 1934.

3A. References 2 and 3.

4. (*a*) Rowe, A. H.: Elimination Diets and the Patient's Allergies: Handbook of Allergy, ed. 2, Philadelphia, Lea & Febiger, 1944. (*b*) Rowe, A. H.: Elimination Diets, ed. 5, Berkeley, Calif., Sather Gate Book Shop, 1958.

5. Rowe, A. H.: Clinical Allergy due to Foods, Inhalants, Contactants, Fungi, Bacteria and Other Causes: Manifestations, Diagnosis, and Treatment, Philadelphia, Lea & Febiger, 1936.

5A. Rowe, A. H., and Rowe, A., Jr.: Allergy and Infection, J. A. M. A. **151:**846-847 (March 7) 1953.

6. Cooke, R. A.: Allergy in Theory and Practice, Philadelphia, W. B. Saunders Company, 1947.

7. Chobot, R.: Infectious Factors in Pediatric and Adult Allergy, J. A. M. A. **150:**1480-1482 (Dec. 13) 1952.

8. (*a*) Rowe, A. H.: Bronchial Asthma due to Food Allergy, in Progress in Allergy, Fortschr. d. Allergielehre, **3:** 222-275, 1952. (*b*) Reference 1*a*.

9. Volwiler, W.: Hypogammaglobulinemic Syndromes, Mod. Med. **26:**83-88 (March 1) 1958. Abernathy, R. S.; Strem, E. L.; and Good, R. A.: Gamma Globulin Treatment of Asthma: Double-Blind Controlled Study, Ann. Allergy, to be published.

10. Rowe, A. H.: Seasonal and Geographic Influences on Food Allergy, J. Allergy **13:**55-62 (Nov.) 1941. Rowe, A. H., and Rowe, A., Jr.: Seasonal and Geographic Influences on Food Allergy, Ann. Allergy, to be published.

11. References 1*b* and 8*a*.

12. Rowe, A. H.: Fever due to Food Allergy, Ann. Allergy **6:**252-259 (May-June) 1948.

13. References 1*c*, 4*b*, and 8*a*.

14. References 1*c* and 8*a*.

HEART DISEASE SCREENING IN ELEMENTARY SCHOOL CHILDREN

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A screening program for the purpose of estimating the prevalence rates for congenital and rheumatic heart disease was carried out among 6,311 children between the ages of 6 and 11 years. Among 165 children thus identified as requiring further study, a secondary program of examinations was carried out. The abnormalities discovered included 33 cases of congenital and 7 of rheumatic heart disease. The study revealed 29 cases of previously unrecognized cardiac abnormality but also relieved at least 15 children of a false diagnosis of heart disease. It was valuable not only in assuring some children of needed treatment but also in determining the diagnostic value of various physical findings.

Pediatric heart disease, in contrast to adult heart disease, is almost invariably associated with chamber enlargement or signs of abnormal cardiac function which enable the abnormal condition to be discovered if sought. Heart disease screening programs are a productive enterprise when conducted among children in a thorough fashion and directed toward detection of the congenital and rheumatic heart defects which are prevalent to varying degrees in various age groups. For instance, congenital heart disease is more prevalent among younger children than among adolescents for the reason that most children with severe defects die before adolescence is reached, although this is counteracted somewhat by the fact that certain of the acyanotic left-to-right shunts (in particular, atrial septal defect) are often not possible to diagnose until the age of 8 to 10 years or even until adolescence. Rheumatic heart disease usually does not appear until 7 to 10 years and is increasingly more prevalent thereafter with advancing age. Thus, there is a difference in the prevalence rates of rheumatic heart disease between populations of younger and older children. The over-all prevalence rate for organic heart disease in children of all ages should be roughly the same, with perhaps a slightly increased rate in adolescents as compared with preschool-aged and elementary school children.

This report is the first of three which will deal with different facets of the entire problem of mass screening for heart disease in children. This paper deals primarily with the results of a screening program in one community and its environs. Prevalence rates of heart disease and innocent murmurs are given, with a discussion of types of disease found, problems encountered, and suggested improvements. The second paper appears on page 1169 of this issue and deals with a comparison of three methods of primary mass screening for heart disease used in two communities. Specificity, sensitivity, efficiency, definitions, and performances are discussed. The third paper [1] compares methods and results of screening programs in two western Colorado communities (different populations than in the second paper), and these results, in turn, are compared with those of previous screening programs by others.

With the Heart Disease Control Program, U. S. Public Health Service, assigned to the Colorado State Department of Public Health (Dr. Morton); Director, Mesa County (Colorado) Department of Public Health (Dr. Beaver); and Chief, Heart Disease Control Program, U. S. Public Health Service (Dr. Arnold). Dr. Morton is now a resident in medicine at San Mateo County Community Hospital, San Mateo, Calif.

Method

The screening program to be described was conducted in Mesa County in western Colorado. The county has a population of about 35,000 to 40,000 persons, of whom about half live in Grand Junction, which is at an elevation of 4,575 ft. above sea level. There is an active, well-staffed county health department and a conscientious, alert medical society. The screening program was coordinated by a physician from the Colorado State Department of Public Health and financed by the Colorado Heart Association.

As many as possible of the accessible elementary school children in the county received a physical examination limited to inspection of the jugular venous pulsations in the neck, palpation of the radial and femoral pulses, inspection and palpation of the chest, auscultation of the heart with the subject in several positions, and blood pressure recordings from the arms and legs if indicated. This comprised the primary screening procedure and was performed by a total of 13 physicians who were experienced in pediatric cardiac auscultation and who worked in teams to facilitate frequent consultations. In addition, lead V_3R electrocardiographic tracings [2] and 70-mm. chest x-rays were obtained from about two-thirds of the children. Three portable electrocardiographs and the state mobile x-ray unit were used for these procedures.

The primary screening phase of the program took place in the Mesa County schools on school days only; it lasted three weeks and covered 6,311 children, most of whom were in the first six grades. All nursing services and organization of volunteers

TABLE 1.—*Age and Sex Distribution of All Children Screened for Heart Disease in Mesa County, Colorado*

	Age, Yr.										
	5	6	7	8	9	10	11	12	13	14+	Total
Male, no. ...	33	442	498	517	526	543	489	145	27	5	3,225
Female, no. .	35	428	491	539	478	510	481	101	19	4	3,086
Total	68	870	989	1,056	1,004	1,053	970	246	46	9	6,311

from the Parent-Teacher Association were provided by the Mesa County Health Department. Twenty-seven schools were covered at 12 separate examining stations, in which children from outlying or smaller schools were brought by bus to the larger and more centrally located schools.

A secondary screening procedure was also carried out in which all children who were thought to have heart disease or to need further evaluation to rule out the presence of heart disease were reexamined by an experienced pediatric cardiologist who was able to utilize complete history, physical examination, electrocardiogram, full-size chest x-ray, and fluoroscopy. Suspicion aroused by results of any of the three screening methods was enough to insure reexamination. This phase of the program required five full days to reexamine 165 children and was followed by letters describing the findings which were sent to the respective personal physicians (M.D.'s and otherwise) in the community.

Results

Of a total population of 6,604 children who were in the first six grades at this time (including two kindergarten classes and a class for retarded children), 6,311 (95.6%) were subjected to a physical examination. There is no information available to characterize the 294 children not examined.

Table 1 reveals a fairly even age and sex distribution for children aged 6 to 11 years, indicating a representative population for these ages. A total of 33 cases of congenital heart disease and 7 of rheumatic heart disease, in addition to several other types of abnormalities, was discovered. Table 2 presents this information in tabular form.

The 33 cases of congenital heart disease included 7 of atrial septal defect, 6 of pulmonary stenosis, 4 of ventricular septal defect, 4 of aortic stenosis, 3 of patent ductus arteriosus, 2 of coarctation of the aorta, and 1 of atrial septal defect combined with pulmonary stenosis. In addition, there was one child with unmistakable arachnodactyly (Marfan's syndrome) who had no detectable heart lesion as yet, one with dextrocardia (with situs inversus), and four with definite congenital heart disease, type undetermined pending cardiac catheterization. In three children a right-sided aortic arch was associated with the primary defect; one had aortic stenosis, one had atrial septal defect, and the other had dextrocardia. The seven children with rheumatic heart disease included five in whom only the mitral valve was involved, one with only the aortic valve involved, and one with both mitral and aortic valves involved.

The child with "other heart disease" was a boy with a long history of severe asthma who was diagnosed as having cor pulmonale on the basis of electrocardiographic evidence of right ventricular hypertrophy. The cor pulmonale could well be reversible and may disappear, since the asthma had no longer been acute during the past year and a half. The three children with electrocardiographic abnormality included one with isolated complete right bundle-branch block (without evidence of

TABLE 2.—*Comparison of Age and Sex With Diagnostic Categories*

		Diagnoses, No.					
			Heart Disease				
Age, Yr.	Sex	Normal	Congenital	Rheumatic	Other	ECG Abnormality	Past Rheumatic Fever	Total
5	M	33	0					33
	F	34	1					35
6	M	438	2	1			1	442
	F	427	0	1			0	428
7	M	492	2				4	498
	F	484	2				5	491
8	M	507	3	0		1	6	517
	F	530	4	1		1	3	539
9	M	524	1			1	0	526
	F	465	2			0	11	478
10	M	526	10		1		6	543
	F	508	1		0		1	510
11	M	487	1	0			1	489
	F	468	3	2			8	481
12	M	144					1	145
	F	100					1	101
13	M	26		1			0	27
	F	17		1			1	19
14+	M	4	0				1	5
	F	3	1				0	4
Totals	M	3,181	19	2	1	2	20	3,225
	F	3,036	14	5	0	1	30	3,086
Both sexes		6,217	33	7	1	3	50	6,311

right ventricular hypertrophy) and two with anomalous muscle bundle between atrium and ventricle (Wolff-Parkinson-White Syndrome).

In addition, there were 50 instances of positive past history of acute rheumatic fever. These 50 cases must not be regarded as any basis for prevalence estimates, since this information was gathered as best it could be from several sources and there is no way of checking the reliability of a history of rheumatic fever.

A certain percentage of these cases of heart disease discovered were already known by virtue of the recently established Mesa County Heart Disease Registry. This registry is kept in the Mesa County Health Department and designed to insure follow-up of those patients supposed to be on a prophylactic regimen against recurrent attacks of rheumatic fever. Another group of cases of heart disease found during the screening program were already known to the children's physicians. However, the majority of the cases of heart disease discovered during the screening program were previously unknown. This information is presented in table 3.

The registry actually is much more adequate than table 3 would indicate. It contained the names of 22 of the 50 children listed as having had rheumatic fever. This incomplete coverage is partly a result of the short time that the registry had been established and partly a result of the reluctance of physicians to fill out report forms. It should be mentioned that three of the children with known congenital heart disease had already had corrective surgery.

The primary reason for collecting figures and recording data was to obtain as good a basis as possible for the estimation of prevalence rates for congenital and rheumatic heart disease in this age group. To have completely reliable figures, one

TABLE 3.—*Comparison of Diagnoses with Previous Knowledge of Heart Disease*

		Mesa County Registry			Other Knowledge, No.		
		Listed, No.					
Heart Disease	Total	Correct Diagnosis	Incorrect Diagnosis	Not Listed, No.	Correct Diagnosis	Incorrect Diagnosis	Not Known, No.
Congenital	33	1	0	32	6	5	21
Rheumatic	7	1	0	6	2	0	4
Other	1	0	0	1	0	0	1
ECG abnormality	3	0	0	3	0	0	3
Total	44	2	0	42	8	5	29

would need a population group large enough to provide at least 50 cases of congenital heart disease and 50 of rheumatic heart disease. Unfortunately, the population being reported is apparently not large enough. However, it is believed the figures obtained should be reported with the caution that larger population studies may report different figures which might be more reliable.

The prevalence rate of a condition is defined as the number of cases of that condition known to exist in a given population at any one time. For this particular prevalence ratio, the numerator will be composed only of the 40 cases of congenital and

TABLE 4.—*Prevalence Rates, in Percentage, of Organic Heart Disease in Elementary School Children*

Heart Disease	Total Population at Risk (6,604)	Examined Population (6,311)
Organic	0.61	0.63
Congenital	0.50	0.52
Rheumatic	0.11	0.11

rheumatic heart disease. The electrocardiographic abnormalities are not included, since they do not constitute organic heart defects. The case of cor pulmonale is not included because it is probably a transient condition. In the choice of a denominator for the prevalence estimate, one could use the total population at risk (6,604) and compute a minimum prevalence rate, or one could use only the population examined (6,311) and compute a maximum prevalence rate. Both sets of prevalence rates are presented in tabular form in table 4.

It may seem to be excessive detail to present both sets of prevalence figures when they are obviously so close, but prevalence estimates have been made from studies based on examinations of a much smaller percentage of the total population at risk. In such instances the two sets of figures represent two ways of regarding the results; they can be further apart; and the difference becomes more significant. The possible significance of the over-all prevalence rate and the rates for rheumatic and congenital heart disease will be discussed in a later paper.

Functional or innocent heart murmurs in children are a fascinating topic, and there is no completely satisfactory explanation for most of them.[3] As with prevalence rates of heart disease, different studies have shown different percentages of the population with an innocent heart murmur. It is probable that most of the differences of opinion about this problem are due to different definitions of terms and to different levels of significance ascribed to what was heard. For the Mesa County program, it was considered advisable to keep a record of all the murmurs heard and their locations. This information is presented in table 5 for all the children without heart disease.

Grade 1 murmurs are included in the records, although no effort was made to keep track of the loudness of the murmurs because of differences in standards and terminology among the examining physicians. Occasional innocent murmurs were as loud as grade 3 on a 6-grade scale. "Venous hums" were included in the group of murmurs heard at the base of the heart. The subdivision of the locations of innocent heart murmurs shown in table 5 was unsatisfactory, since it was noted during the screening program to be not adequately subdivided

as to locations and, in some, for sound quality. Perhaps a mimeographed diagram of the precordium should have been included on the record card. This would have permitted more exact differentiation of the location of the innocent murmurs and would have been worth the effort.

A facet of the innocent heart murmur that could stand further clarification is the quality of the sound. "Vibratory" is the term most commonly accepted in the Rocky Mountain area [4] to describe the sound quality of the classic innocent murmur; this denotes a relatively pure sound accompanied by harmonious overtones. However, these murmurs are often composed of disharmonious overtones, and all are not "vibratory" in quality. Some have a definite blowing quality, others are slightly rough, and others are squeaky. This is really a problem in semantics. Although the pitch of the innocent murmur is usually described as low, this is a characteristic of the innocent murmur that often is not too closely attended. To those of us without a phonocardiogram, pitch may most readily be determined by the relative difference between the sound as heard through the diaphragm of the stethoscope (high-pitched sounds are heard relatively better) and the sound as heard through the bell of the stethoscope (low-pitched sounds are heard relatively better). Although probably many functional heart murmurs are indeed low-pitched, many must be called medium-pitched.

The great hallmark of the innocent heart murmur is its variability with respiratory and positional changes. The murmur may completely disappear during a moderately deep, held inspiration, while "organic" murmurs do not. The murmur may be audible when the subject is in the recumbent position and not when he is in the erect position or, rarely, vice versa. The point where the murmur is heard loudest often shifts considerably when the subject's position changes. Exertion may accentuate or diminish the murmur. Anxiety mimics the effects of exertion, especially in children.

Table 5 shows that there are more boys than girls with functional heart murmur. There were also more boys screened than girls. However, among the children 10 and 11 years old, more girls than boys had murmurs. It is doubtful that the totals of each sex in each age group are large enough to be conclusive in this regard. The over-all percentage of innocent heart murmurs heard in normal children in this study (33%) agrees well with percentages found in previous similar studies on Colorado children: 30% of 1,617 elementary school children [2] and 36% of 11,236 sixth graders.[5]

TABLE 5.—*Comparison of Age and Sex with Innocent Heart Murmurs and Their Locations*

Age, Yr.	Sex	Murmurs,* No.							
		None	Base	L.S.B.	L.S.B. and Base	L.S.B. and Apex	W.P.	Total Murmurs	Total
5	M	12	0	9	4	4	3	20	32
	F	23	1	6	1	2	1	11	34
6	M	282	29	76	6	31	15	157	439
	F	290	23	74	9	18	13	137	427
7	M	311	27	103	4	36	16	186	497
	F	340	32	72	7	24	14	149	489
8	M	344	26	101	6	25	11	169	513
	F	380	31	79	12	21	10	153	533
9	M	361	25	90	9	21	18	163	524
	F	354	24	65	6	16	9	120	474
10	M	358	28	109	3	24	14	178	536
	F	319	46	98	14	17	14	189	508
11	M	336	33	73	12	26	9	153	489
	F	307	36	97	9	15	12	169	476
12	M	94	5	34	0	10	2	51	145
	F	54	10	29	2	3	3	47	101
13	M	19	1	3	0	1	2	7	26
	F	13	2	3	0	0	0	5	18
14 or older	M	2	0	3	0	0	0	3	5
	F	2	0	1	0	0	0	1	3
Totals	M	2,119	174	601	44	178	90	1,087	3,206
	F	2,082	205	524	60	116	76	981	3,063
Both sexes		4,201	379	1,125	104	294	116	2,068	6,269

* L.S.B. = left sternal border; W.P. = whole precordium.

This fact would suggest a certain degree of comparability with the previous studies.

No effort was made to obtain statistics on variations in heart sounds heard during the screening program. In particular, the respiratory variation in the splitting of the second heart sound as heard in the second left intercostal space was a closely attended phenomenon during each auscultation. Especially in children, the second heart sound in the "pulmonary area" usually is split during inspiration and single or less widely split during expiration.[6] During this and previous screening activities, it was noted that this split varied in normal children from being only occasionally heard during inspirations to a practically constant wide splitting during expirations. Of course, the loudness of the second sound is of considerable assistance in judging the normality of the respiratory splitting which is significant, since pulmonary hypertension will usually cause a loud and often snapping second

heart sound with loss of the respiratory variations in splitting and a fixed reduplication. In addition, a constantly pure second sound in the pulmonary area may be a feature of pulmonary or aortic stenosis, although this has been reported to be an inconstant phenomenon.[7] Inspiratory splitting of the first heart sound along the lower left sternal border and at the apex was another event that could have been recorded. Perhaps another similar study could shed more light on the normal variations and occurrence of heart sounds as well as heart murmurs. This problem is of particular interest because heart sounds are often of more value in identification of heart disease than heart murmurs. Indeed, heart murmurs are usually judged by the accompanying sounds.

It is interesting to note what was advised as to recommendations for the children who were reexamined. This is shown in table 6. The recommendations were made with primary attention to which course of action would be the most practical in a community 260 miles away from where cardiac catheterization could be done. In addition, two of the children with congenital defects were being followed for serious primary mental deficiencies as well, and it was considered that expensive corrective procedures were best deferred in these instances.

Comment

Most physicians work with patients who come or are brought to them with a complaint. In the field of pediatric heart disease this means that, by the time the physician sees the patient, the patient usually has fairly characteristic signs of illness from which a diagnosis may be extracted. As might be expected, a screening program will tend to discover patients in an earlier stage of the progression of their condition. This means that often the diagnostic signs will be more equivocal in the patient with previously unknown heart disease than at a later date when symptoms might have caused him to seek a physician's care. This phenomenon is especially apparent in congenital heart disease wherein there are wide variations in the rate of progression of the condition and its complications, depending on the extent of the defect and on unknown factors in the constitution of the patient. In this study, as in a previous one,[2] relatively mild degrees of congenital defects without functional impairment, such as localized ventricular septal defect (Roger's disease) or some cases of atrial septal defect, pulmonary stenosis, and aortic stenosis, are included as definite congenital heart disease because knowledge at present cannot definitely rule out the possibility that these persons may some day have disability as a result of their defect. This is also the line of reasoning responsible for classifying the case of arachnodactyly as congenital heart disease, even though there is as yet no demonstrable defect. In congenital heart lesions, it is particularly important to discover defects (especially shunts) before irreversible pulmonary hypertension has set in, so that life will actually be prolonged by corrective surgery.

The case of one 7-year-old girl, included in the "normal" category in table 2, may illustrate a phenomenon recently described by Silber,[8] who mentions that viral carditis may produce transient murmurs identical with those of rheumatic heart disease. At the time of the primary screening examination, the girl had had a low-grade fever and wet cough, that had been present for about two weeks, some lassitude, and a grade 3, blowing, high-pitched pansystolic murmur heard all over the precordium, loudest at the apex, radiating to the left axilla, and accompanied by a muffled first heart sound in the "mitral area." Intermittent rhonchi were heard over both lung fields. There was no other history of any other manifestations of rheumatic fever, her sedimentation rate was normal, and her family history was negative. Although this does not rule out the supposed entity of subclinical rheumatic fever, there was no acute episode of rheumatic fever to account for the very definite and previously unheard murmur of mitral insufficiency. Four weeks later, when she was reexamined by the pediatric cardiologist in conjunction with the screening physician, it was readily agreed that the patient had a grade 2, vibratory, low-pitched systolic murmur heard all over the precordium, loudest in the fourth left intercostal space, and not heard in the left axilla. At this time the first heart sound was entirely normal, there was no indication of upper or lower respiratory tract infection, and the heart murmur was judged to be classically innocent. In the interval between the examinations, the patient had been receiving orally one penicillin tablet per day, but no anti-inflammatory drugs, and she had not been kept home from school. Of course the possibility of an endocarditis has not been ruled out, although this is a little remote considering the

TABLE 6.—*Comparison of Diagnostic Categories with Recommendations in Discovered Cases of Heart Disease*

		Other Studies Needed						Surgery		
				Reexamination After					Depending on Result of Cardiac Catheterization	
	Total	None	Cardiac Catheterization	1 Yr.	2 Yr.	5 Yr.	No	Yes		Already Done
Heart disease										
Congenital..	33	8	14		10	1	14	6	10	3
Rheumatic..	7		1	5	1		6		1	
Other.....	1				1		1			
ECG abnormality.....	3	3					3			
History of rheumatic fever.....	50			1	49		50			
No heart disease.....	71	58		1	12		71			
Total.....	165	69	15	7	73	1	145	6	11	3

clinical course. Since a virus or its antibody response was not definitely identified, the case is open to speculation, but the hypothesis of transient viral carditis is interesting and thought-provoking.

The physicians of this Colorado town are, as a group, probably as well-trained and able to diagnose heart disease as any other comparable group in the United States. Thus, the fact that 29 of these 43 cases of heart abnormalities were previously unrecognized is no reflection on the local medical practice. As previously mentioned, most of those children were not having the symptoms or signs of illness that would cause their parents to seek medical attention. In addition, many of the incorrect previous diagnoses mentioned in table 3 had been made by paramedical personnel in the community (who seem interested in heart disease but not as well trained in the subject).

One discouraging facet of this sort of program is that not all the subjects in whom heart disease is discovered will receive the recommended diagnostic studies or corrective operation. In fact, from past experience gleaned from other similar surveys, probably only about one-half of those who have not already had an operation and in whom disease was discovered in this survey will actually receive the benefit of the available therapeutic potential in time to really prolong life to somewhere around the normal expectation. There are many reasons for this, most of them sociological: parental maladjustments, distrust of doctors, financial embarrassment, refusal to accept the free care available, and other factors. Cases of acyanotic congenital heart disease are particularly apt to result this way because the children "don't look sick" to the parents. By the time they do look sick enough, it is often too late in the progression of the disease to obtain a cure by operation; either the patient is too poor a surgical risk, or irreversible pulmonary vascular changes have occurred. This sort of thing is probably more apt to happen in a rural then an urban population.

It is as important to avoid overdiagnosis as underdiagnosis. The production of excessive anxiety concerning the heart should be avoided if possible. That considerable anxiety is generated in the children by such a screening procedure is apparent when one discovers later from teachers and parents what comments the children have made and to what lengths they sometimes go to avoid the screening procedure.

It can be readily seen that the discovery of previously unknown cases of heart disease is a significant event. Children with rheumatic heart disease may be placed on a prophylactic regimen against recurrent attacks of rheumatic fever, and children with congenital heart disease may undergo corrective operation or may be given follow-up examinations until such time as the development of symptoms or signs of dysfunction might make operation desirable. However, the other side of the coin is that there were at least 15 children who were relieved of a false diagnosis of heart disease. This is a minimum figure, since this result was not anticipated and the records kept did not include previous diagnoses on all the normal children. These children were usually on rather severely restricted activity regimens and in some cases were real behavior problems in school and at home, utilizing their supposed heart defect to immunize themselves against punishment. However, it is possible that some of these children received their diagnosis during an episode of illness similar in effect to the one described in the 7-year-old girl with an upper respiratory infection. The possibilities for error make it necessary to examine a child at least twice before making a definite diagnosis of heart disease.

Summary

In a screening program for heart disease in elementary school children, 33 cases of congenital heart disease and 7 of rheumatic heart disease were discovered in a total population of 6,604 children, 95.6% of whom were examined. Other types of heart abnormality were also found. Of the children without heart disease, 33% had innocent heart murmurs.

222 39th Ave., San Mateo, Calif. (Dr. Morton).

This study was supported by a grant from the Colorado Heart Association. Examining physicians were provided by the Heart Disease Control Program of the U. S. Public Health Service, the National Jewish Hospital, Denver, and the University of Colorado Medical Center. Nurses and auxiliary personnel were provided by the Mesa County (Colorado) Department of Public Health. Record analysis and guidance were provided by the Colorado State Department of Public Health.

References

1. Morton, W., and Dodge, H. J.: Comparison of Pediatric Heart Disease Found in Two Communities, to be published.

2. Morton, W.; Lloyd, L.; Dodge, H. J.; and Hoffman, M. S.: Use of Single-Lead ECG in Detection of Congenital Heart Disease, A. M. A. J. Dis. Child. **95:**492-497 (May) 1958.

3. Luisada, A. A., and others: Murmurs in Children: Clinical and Graphic Study in 500 Children of School Age, Ann. Int. Med. **48:**597-615 (March) 1958.

4. Rhodes, P. H.: Diagnosis of Innocent Heart Murmurs in Children, GP **12:**69-71 (Aug.) 1955.

5. Maresh, G. J.; Dodge, H. J.; and Lichty, J. A.: Incidence of Heart Disease Among Colorado School Children: State-Wide Study, J. A. M. A. **149:**802-805 (June 28) 1952.

6. Warren, J. V.; Leonard, J. J.; and Weissler, A. M.: Gallop Rhythm, Ann. Int. Med. **48:**580-596 (March) 1958.

7. Ongley, P. A., and others: Aortic Stenosis in Infants and Children, Pediatrics **21:**207-220 (Feb.) 1958.

8. Silber, E. N.: Respiratory Viruses and Heart Disease, Ann. Int. Med. **48:**228-241 (Feb.) 1958.

COMPARISON OF THREE METHODS OF SCREENING FOR PEDIATRIC HEART DISEASE

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and
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Three screening methods were compared as to specificity and sensitiveness in the detection of cardiac abnormalities by applying them to each of 5,654 children. The three methods consisted of a single-lead (V_3R) electrocardiogram, a miniature chest roentgenogram, and a limited physical examination. For each method it was possible to define a sensitivity index, a specificity index, and their product, an efficiency index. The V_3R gave a specificity index of 0.190 (ratio of true positive to total positive findings), and of 58 children with abnormal V_3R tracings 44 had normal hearts. The physical examination, used singly, was the most specific and the most sensitive and gave the highest efficiency index, but none of the methods was infallible.

Screening methods for the purpose of detecting heart disease have received extensive evaluation in adults. Screening programs with use of chest x-ray, brief history, limited physical examination, blood pressure recordings, and electrocardiogram singly or in combination have been described.[1] In adults, rheumatic heart disease and hypertensive heart disease are more readily discovered by screening, but arteriosclerotic heart disease (the major problem) is considerably more difficult to detect on a screening basis unless angina pectoris is present or a myocardial infarction has occurred, and even then detection of disease is not easy. It has also been the experience in previous studies that incipient or even frank cor pulmonale in adults is difficult to detect on a screening basis.

However, in children, the problem of screening for heart disease is made easier by the fact that the two commonest types of heart disease, congenital and rheumatic, generally produce specific chamber enlargement, pulmonary vascular changes, or characteristic heart murmurs which produce definite auscultatory electrocardiographic, or radiologic signs.

Increased consciousness of heart disease on the part of the general public, the development of corrective surgery for various types of heart disease, and the development of effective prophylaxis against recurrent attacks of rheumatic fever have made the discovery of heart disease among children a valid community public health activity. This is especially true since most physicians have neither the time nor the desire (and often not the experience) to screen hundreds and sometimes thousands of children to weed out the approximately 0.5 to 1.0% of children who have heart disease and who will benefit from medical attention.

There is a need for more information regarding the sensitivity, specificity, and reliability of the various methods which might be used singly or in combination in screening for pediatric heart disease. Estimates of these must be based on studies of large populations of children in which all have been checked by the best other method in addition to the one being tested. For purposes of statistical validity, it is estimated that the population should be large enough to yield at least 50 cases of heart disease, which would mean that at least 5,000 to 10,000 children should be screened to test any given method.

The only real practical check available to evaluate the various screening methods is the total evaluation, including history, careful physical examination by physicians experienced in cardiac diagnosis, electrocardiogram, x-ray, and, at times, selected physiological tests. It becomes apparent that the problem of evaluation of a single diagnostic test is a difficult process. The primary purpose of this paper is to present the information obtained from three screening methods used simultaneously on the same group of grade school children.

Method

Over a period of two school years in two western Colorado communities, a total of 5,654 grade school children were examined by single-lead electrocardiogram, miniature chest x-ray, and limited physical examination. A total of 7,928 children were examined by at least one method, but only 5,654 were subjected to all three screening methods. The prevalence rates noted for heart disease and innocent

With the Heart Disease Control Program, U. S. Public Health Service, assigned to the Colorado State Department of Public Health (Dr. Morton); Chief of Cardiology, National Jewish Hospital (Dr. Hoffman); Executive Director, Colorado State Department of Public Health (Dr. Cleere); and acting head of the Department of Preventive Medicine, University of Colorado Medical Center (Dr. Dodge). Dr. Morton is now a resident in medicine at San Mateo County Community Hospital, San Mateo, Calif. Dr. Dodge is now Professor of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Mich.

heart murmurs have been reported elsewhere,[3] and this report will concentrate on the comparison of sensitivity and specificity of the three methods used.

The primary physical examination was performed by selected physicians experienced in cardiac diagnosis; it consisted of inspection of the jugular venous pulses, palpation of the radial and femoral arterial pulses, inspection and palpation of the chest, and auscultation of the heart with the child in several positions and with attention to respiratory variations in heart sounds. Blood pressure recordings from arms and legs were obtained when indicated by heart sounds or arterial pulse characteristics.

TABLE 1.—*Comparison of Processing Rates for Three Screening Methods for Heart Disease*

Primary Screening Test	Personnel Required	Children Examined per School Day, No.	Results Read per Hr., No.
Physical examination (1 team of 2 M.D.'s)	2 physicians, 1 nurse, 2 PTA mothers	300-400	Immediate
ECG, V_3R lead (1 machine)	1 trained nurse or technician, 2 PTA mothers	200-300	500-600
70-mm. chest x-ray (mobile unit)	2 technicians and 2 PTA mothers or 1 technician and 3 PTA mothers	500-600	400-500

The single V_3R lead of the electrocardiogram was used as a screening tool because a large proportion of the congenital heart defects found in this age group are conditions associated with right ventricular hypertrophy, most readily detected by right precordial leads. Two criteria for this abnormality were used: (1) ratio of R wave to S wave greater than unity and (2) ventricular activation time (from onset of QRS complex to peak of tallest R wave) of 0.04 seconds or longer. If both criteria were present, the tracing was considered abnormal. If only one criterion was present, the finding was considered borderline. The tracings were obtained by registered nurses who were trained for this task, and they were assisted by mothers from the Parent-Teacher Association. Alcohol sponges were used in place of electrode paste to save time.

The state mobile x-ray unit, ordinarily devoted to screening for tuberculosis, was used to obtain 70-mm. chest x-rays. The x-rays obtained in the heart disease screening program were also examined for tuberculosis, and as a result 10 children were suspected of having the latter disease. Children were noted by the technicians to require more effort to x-ray than adults, and the smallest children stood on various sized boxes in order to reach the screen. Since the screening procedures were organized to be performed in rapid succession on the same children, it was necessary to know the rate at which children could be processed. Table 1 presents the maximum performance rates for the three methods. The PTA mothers listed under personnel are used for dressing and undressing children, keeping noise down to a reasonable level, seeing that no children are overlooked, and similar needs. Usually the children are brought to the examining site by class, and the teachers are also present.

Actual organization of screening schedules and auxiliary personnel was done by the public health and school nurses from the local health departments. One or two nurses were always present during the screening procedure. The entire program was coordinated by the Heart Disease Control Program of the Colorado State Department of Public Health and financed by the Colorado Heart Association. Screening physicians were provided largely from Denver, although there was some participation by interested physicians in each community.

As a result of the primary screening phase of the program, any child screened out by any of the three methods was reexamined by a pediatric cardiologist who utilized complete history, physical examination, electrocardiogram, full-size chest x-rays, fluoroscopy, and, at times, such physiological procedure as heart catheterization. The parents were told of the findings on the spot, and, in addition, letters were mailed to family physicians describing the findings, the probable diagnosis, and any further recommendations.

Results

Table 2 shows the age and sex distribution of the children screened for heart disease by all three methods. From this table, it may be seen that a representative population (with respect to age and sex distribution) of grade school children was screened.

Accumulating the results of all three screening methods, this population of 5,654 children included 36 with congenital heart disease, 5 with rheumatic heart disease, 1 with "other" heart disease (cor pulmonale), and three with electrocardiographic abnormality without organic heart disease; 5,609 children were normal.

Since the V_3R lead was used to detect right ventricular hypertrophy only, the children were divided into those with this condition and all others. The child with "other" heart disease happened to have right ventricular hypertrophy. The three cases of electrocardiographic abnormality without organic heart disease consisted of two of anomalous muscle bundle between atrium and ventricle (Wolff-Parkinson-White syndrome) and one of isolated, complete, right bundle-branch block. The children with rheumatic heart disease all had mitral valve involvement only. The cases of congenital heart disease

TABLE 2.—*Comparison of Age and Sex of Children Screened for Heart Disease*

	Age, Yr.									
Sex	5	6	7	8	9	10	11	12	13+	Total
Male, no.	2	468	477	465	498	455	403	110	16	2,894
Female, no.	4	438	477	481	455	417	384	90	14	2,760
Total	6	906	954	946	953	872	787	200	30	5,654

consisted of 10 of atrial septal defect, 5 of ventricular septal defect, 5 of aortic stenosis, 5 of pulmonary stenosis, 3 of patent ductus arteriosus, 2 of coarctation of the aorta, 1 of arachnodactyly (Marfan's syndrome), 1 of dextrocardia, 1 of tetralogy of Fallot, and 3 of congenital heart disease, type unknown.

When considering the number of different screening methods, it is helpful to consider the specificity of the tests for a condition and the sensitivity of the tests in detecting the condition. These terms give a numerical measure of the tests. Thus, the following definitions of terms are in order: 1. Specificity. A test is wholly specific when the result is positive only in the presence of the condition for which the test is made. The measure of specificity is the ratio of true positive tests to total positive tests. 2. Sensitivity. A test is wholly sensitive when the result is invariably positive in the presence of the condition for which the test is made. The measure of sensitivity is the ratio of true positive tests to the total number of patients having the condition for which the test is made. 3. Efficiency. In order to have some expression which will combine specificity and sensitivity, an index of efficiency is calculated by multiplying the ratios of specificity and sensitivity.

A screening test with a relatively high sensitivity may have a relatively low specificity and vice versa. By inspection of table 3, it will be seen that all the screening methods missed cases of heart disease (false-negative results) and all gave a certain proportion of false-positive results. It is helpful to assemble these figures in another table (table 4) for comparison.

TABLE 3.—*Comparison of Diagnostic Categories with Results of Three Methods of Screening for Heart Disease*

		Results, No.							
		Physical Examination		ECG, V_3R Lead			Chest X-ray, 70 Mm.		
Diagnosis	Total	Positive	Negative	Abnormal	Borderline	Normal	Positive	Negative
Congenital heart disease									
Right ventricular hypertrophy	13	10	3	11	1	1	7	6
Other	23	20	3	0	5	18	5	18
Rheumatic heart disease	5	5	0	0	0	5	3	2
Other heart disease (cor pulmonale)	1	0	1	0	1	0	0	1
ECG abnormality	3	0	3	3	0	0	0	3
Normal	5,609	72	5,537	44	437	5,128	41	5,568
Total	5,654	107	5,547	58	444	5,152	56	5,598

It is interesting to note that seven cases of heart disease would have been missed by use of the physical examination alone. In judging the V_3R lead, only the "abnormal" category was considered as positive in computing the specificity, and only the cases of right ventricular hypertrophy were considered in computing the sensitivity. As has probably been noticed, table 4 was computed on the assumption that the screening program discovered all the cases of heart disease within the population of 5,654 children. This is only an assumption, because cases could have been missed even with the simultaneous use of three screening tests. The only way to gain a more reliable foundation for this sort of work would be to examine every one of a population of several thousand children at a diagnostic center where they would receive a complete diagnostic study, including fluoroscopy.

TABLE 4.—*Comparison of Specificity, Sensitivity, and Efficiency of Three Screening Methods, Used Alone and in Combination*

	Specificity†		Sensitivity‡		
Method*	Ratio	Quotient	Ratio	Quotient	Index of Efficiency§
Physical examination	35:107	0.327	35:42	0.833	0.272
ECG, V_3R lead	11:58	0.190	11:14	0.786	0.149
Chest x-ray, 70 mm.	15:56	0.268	15:42	0.357	0.096
Physical examination plus ECG	37:150	0.247	37:42	0.881	0.218
Physical examination plus x-ray	37:152	0.243	37:42	0.881	0.214
Chest x-ray plus ECG	20:107	0.187	20:42	0.476	0.093

* All methods except that with ECG alone (for right ventricular hypertrophy) computed for all heart disease.
† Ratio of true positive tests to total positive tests.
‡ Ratio of true positive tests to total number of subjects with condition for which test is done.
§ Ratios for specificity and sensitivity multiplied.

Of the three screening methods used singly, the physical examination was the most specific, although all methods were fairly close in this respect and produced many false-positive results. The V_3R lead was the least specific, even though it was only judged in the detection of right ventricular hypertrophy. The physical examination was also the most sensitive, with the V_3R lead a close second (only in the detection of right ventricular hypertrophy) and the 70-mm. chest x-ray a poor third. Thus, the physical examination seemed to be the most efficient screening method.

Inspection of the tabular comparison between the various combinations of screening methods (table 4) shows that, although use of the physical examination in conjunction with either the V_3R lead or the 70-mm. chest x-ray will increase the sensitivity of the screening program, the specificity would then fall below the value obtained when only the physical examination is used as a screening method. Of course, the combination of all three screening methods used simultaneously is even more sensitive but less specific than the physical examination used alone. However, there is nothing against which to measure the over-all sensitivity of the entire screening program in this study.

Comment

It must be remembered that these screening programs were conducted afresh in each community and that, if this program were set up on a continuing basis with the community physicians gaining experience in screening for heart disease each year, the values presented for specificity, sensitivity, and efficiency of the screening program should rise. Also, it would certainly be much more advantageous

in respect to time and finances to screen for heart disease with use of only one screening method instead of three. At the most, two methods might be used simultaneously.

The V_3R lead was fairly sensitive in the detection of right ventricular hypertrophy, and considerable moral support was given to the screening physicians when the tracing was taken just before the physical examination and attached to the child's record card. It must be pointed out that the electrocardiographic criteria used herein for the diagnosis of right ventricular hypertrophy were limited by the technique, in that such patterns as deep S waves in the left precordial leads or shift in precordial transitional zone to the left could not be used to make this diagnosis. Had complete electrocardiographic tracings been obtained on each of these children and read for right ventricular hypertrophy, the screening method would probably have been more sensitive but would have lost a good deal of specificity. It should be emphasized that, of the 58 children with abnormal V_3R tracings, as judged by rather strict standards, only 11 had right ventricular hypertrophy, 3 had electrocardiographic abnormalities, and 44 had normal hearts. The 44 normal children with electrocardiographic evidence of right ventricular hypertrophy should cause one to reflect that the electrocardiogram is an ancillary and not a primary diagnostic tool. However, it would seem to be an advantage to have electrocardiographic assistance in the diagnosis of conditions which might cause left ventricular hypertrophy or combined ventricular hypertrophy. A complete electrocardiogram would probably complicate the record handling and interpretation procedures too much to be of that much additional value. However, since the child is already "wired" for a chest lead, perhaps one or maybe two additional leads could be recorded and judged by definite criteria without loss of the relative simplicity of the procedure.

The chest x-ray is not a sensitive tool with which to detect heart disease, especially in children, most of whom are in an early stage of their disease. It is certainly an excellent means, however, of following changes in heart size and configuration and in pulmonary vascularity in patients whose heart disease is already known. X-rays are also invaluable in making a diagnosis of heart disease. The screening efficiency of the x-ray was decreased by the fact that there is a wide range of normal appearance of the heart contour. This, coupled with the fact that many of the subjects screened had no gross cardiac enlargement, made the method less desirable for this purpose in this age group. In view of the cost and size of x-ray equipment, the chest x-ray probably does not have as much developmental potential as a mass screening tool as other methods.

This study, with simultaneous use of three screening procedures, has established one fact: no screening method is infallible. Even in the physical examination, when performed by experts, heart disease can be overlooked in an age group in which it has previously been thought that heart disease should not be missed. This has a bearing on past studies of prevalence rates of heart disease in this age group, which have usually been based on the physical examination. It means that, if the studies were performed on large enough groups of children (over 5,000), the prevalence rates offered probably erred on the low side of the true prevalence rates.

Recently, several investigators have been developing the phonocardiogram with heart sound recordings on hi-fi tape as a mass screening tool for discovering heart disease among children. The phonocardiogram operated by a technician would save physicians' time and make possible the screening of a large number of children with minimum expense. It must be remembered that the phonocardiogram as used in this fashion would be an ancillary tool, as are the electrocardiogram and the chest x-ray, and it should not be expected to measure up to the results of a screening program with trained physicians who use their hands and eyes in addition to their ears. This is merely to caution against overenthusiasm for a new tool and not to detract from the many obvious advantages of working with a phonocardiogram in this fashion.

The population of 5,654 children in this study cannot be used in computing prevalence rates of heart disease, since it was arbitrarily selected from a larger group of 7,928 children screened. The group discussed in this paper was selected solely on the basis of having had all three screening procedures performed.

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References

1. (*a*) Rutstein, D. D.: Screening Tests in Mass Surveys and Their Use in Heart Disease Case Finding, Circulation **4**:659-665 (Nov.) 1951. (*b*) Dawber, T. R.; Kannel, W. B.; Love, D. E.; and Streeper, R. B.: Electrocardiogram in Heart Disease Detection: Comparison of Multiple and Single Lead Procedures, ibid. **5**:559-566 (April) 1952. (*c*) Phillips, E.; Chapman, J. M.; and Goerke, L. S.: Relative Values of Techniques Used in Detection of Heart Disease, Am. Heart J. **45**:319-330 (March) 1953. (*d*) Morton, W.; Lloyd, L.; Dodge, H. J.; and Hoffman, M. S.: Use of Single-Lead ECG in Detection of Congenital Heart Disease, A. M. A. J. Dis. Child. **95**:492-497 (May) 1958. (*e*) Witham, A. C., and Coggins, R. P.: Electrocardiographic Technique for Mass Surveys, Am. Heart J. **51**:199-210 (Feb.) 1956. (*f*) Kurlander, A. B.; Hill, E. H.; and Enterline, P. E.: Evaluation of Some Commonly Used Screening Tests for Heart Disease and Hypertension, J. Chron. Dis. **2**:427-439 (Oct.) 1955. (*g*) Witham, A. C., and Jones, H. B.: Relative Value of Electrocardiography and Photoroentgenography for Cardiac Surveys, Am. Heart J. **51**:186-198 (Feb.) 1956. (*h*) Ireland, C. R.; Witham, A. C.; and Harper, H. T., Jr.: Congenital Heart Disease Among Mental Defectives and Assessment of Cardiac Survey Methods, New England J. Med. **252**:117-125 (Jan. 27) 1955.

2. Morton, W.; Beaver, M. E. N.; and Arnold, R. C.: Heart Disease Screening in Elementary School Children, J. A. M. A. **169**:1163-1168 (March 14) 1959.

INTRAVENOUS USE OF OXYTOCIN (PITOCIN) FOR INDUCTION OF LABOR

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The extent to which oxytocin is being used to initiate or stimulate uterine contractions in labor was investigated by analyzing certain information on birth and fetal death certificates in New York City. Of 165,150 live births in 1955, 7,694 (4.7%) were induced with intravenously given oxytocin. In 1956 the over-all reported incidence rose to 5.0%. Three case-histories are given to illustrate the irrational use of this drug. The data showed that its use was influenced by the season of the year and by the socioeconomic status of the patient and that in cesarean sections and breech deliveries the prior use of oxytocin increased the infant mortality.

Posterior pituitary products, administered intramuscularly, were used in obstetrics for many decades for the induction and/or stimulation of labor. A new modality, oxytocin (Pitocin), diluted for intravenous use, was first suggested for stimulation and induction of labor by Page [1] in 1943. His report was followed in 1949-1950 by the clinical reports of Theobald and others [2] and Hellman [3] on dilute oxytocin in 5% glucose solution (1:5,000 to 1:7,000), given intravenously. These reports initiated the widespread use of oxytocin for the induction and stimulation of labor. An ever-increasing trend in this usage is attested by subsequent reports in the literature.[4]

Many questions, such as the following, need to be raised regarding the possible deleterious effects of intravenously given oxytocin. 1. Does it increase the incidence of ruptured uterus? 2. Does it increase the incidence of premature separation of the placenta? 3. Does it increase uterine hemorrhage? 4. Does it increase the incidence of prematurity? 5. Does it increase perinatal mortality? 6. Is it harmful in a breech presentation? 7. Is the infant unduly traumatized? 8. Does it produce fetal anoxia with resultant central nervous system damage that may not be ascertained until years later?

Published studies [5] on intravenously given oxytocin have been confined to an individual hospital or group of hospitals where careful supervision usually prevails. These sources indicate that with proper control this method does not significantly increase the hazard to mother or infant. In an effort to determine the extent of usage and to obtain additional information about the questions raised, this present study was initiated.

Method of Study

This report is based on an analysis of birth and fetal death certificates from New York City for 1955-1956 (see figure). These certificates request the following information: 1. Was induction attempted? 2. Indication? 3. Method of induction? 4. Successful? ("Successful" is interpreted as the initiation of active labor resulting in birth per vaginam.) These items were coded and punched on I. B. M. cards. The coding was set up as shown in table 1.

For the purpose of this study, all certificates coded 4, 5, or 6, which refer to the induction of labor with oxytocin, were included, and the tabulations were limited to these. If oxytocin was stated to be used for "stimulation of labor," then codes 4, 5, or 6 were not utilized and these cases were not included. Information regarding acceleration (or stimulation) of labor is not available from the birth certificate. Failure to answer one or more of the questions on the birth certificate regarding the use of intravenously given oxytocin is recognized as a limitation in this analysis. Many cases of induction are categorized as resulting from "stimulation," and, therefore, the actual incidence is underreported. Information and correlations were obtained which are of interest and which may serve to stimulate further clinical studies relating to the use of intravenously given oxytocin.

Additional information was obtained from a questionnaire sent to all the directors of obstetric services of hospitals in New York City. This requested information on live births and fetal deaths occurring on the private and ward services, with regard to the use of intravenously given oxytocin for the stimulation and induction of labor. A response was obtained from 79 hospitals, for 1955, with a total of 128,324 live births. These included 49 voluntary, 16 proprietary, and 14 municipal hospitals. A similar questionnaire was sent for the year 1956, was completed by 83 hospitals, and resulted in information on 136,451 live births.

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Registry of Births

2-M (Rev. 9/57) 312500-701350(57) 10

1. Name of child
2. Sex — 3. No. of children born of this pregnancy — 4. No. of this child in order of birth
5. Date of birth — Hour — A.M. P.M.
6. Place of birth — Boro
7. Residence of mother: State — County
Post Office and Zone
Address
8. FATHER: Name
9. Color — 10. Age — 11. Birthplace
12a. Usual Occupation
12b. Kind of business or industry in which work was done
13. MOTHER: Maiden name
14. Color — 15. Age — 16. Birthplace
17a. Total number of children BORN ALIVE PREVIOUS to this pregnancy
17b. Number of children born PREVIOUS to this pregnancy and NOW LIVING
Date of return

2-M (Rev. 9/57) 10

THIS CERTIFICATE NOT VALID UNLESS FILED IN THE HEALTH DEPARTMENT
DO NOT WRITE IN THIS SPACE. MARGIN RESERVED FOR CODING AND BINDING

Boro Birth
Instit.
Boro Resid.
Area Dist.
S C N
FATHER Age Nat.
MOTHER Age Nat.
Total Births
Born Alive
Now Living
Stillborn
Attendant
Mail. Inj.
Gestation Wks.
Weight Lbs. Oz.

Cert. No.
Place
Died. Date

Certificate of Birth

FILED

Certificate No.

1. Full name of child (PRINT) — First name — Middle name — Last name
2. Sex — 3. Number of children born of this pregnancy — 4. If more than one, number of this child in order of birth
5. Date of child's birth (Month) (Day) (Year) — 5a. Hour — A.M. P.M.
6. PLACE OF BIRTH
(a) NEW YORK CITY: (b) Borough
(c) Name of Hospital or Institution
(d) If not in hospital, street address No. — Ave.
7. USUAL RESIDENCE OF MOTHER:
(a) State
(b) Co. — (c) City or Town
(d) No. — Ave. St.

FATHER — MOTHER

8. Full name
9. Color or race — 10. Age at time of this birth (years)
11. Birthplace (city or place and State, or country)
12a. Usual Occupation
12b. Kind of business or industry in which work was done
13. Full maiden name
14. Color or race — 15. Age at time of this birth (years)
16. Birthplace (city or place and State, or country)
17a. Total number of children BORN ALIVE PREVIOUS to this pregnancy
17b. Number of children born PREVIOUS to this pregnancy and NOW LIVING

I hereby certify that this child was born alive at the hour and on the date stated above, and that all the facts stated in this certificate and report of birth are true to the best of my knowledge, information and belief.

(Signed) ....., M.D. R.N. D.O.
Address .....
Date of Report 19

Given name added from a supplemental report (Date of)
Borough Registrar.

Print here the mailing address of mother. ➡
Copy of this certificate will be mailed to her when it is filed with the Department of Health.

Name .....
Address ..... Apt. Post Office Zone
City ..... State .....

BUREAU OF RECORDS AND STATISTICS — DEPARTMENT OF HEALTH — THE CITY OF NEW YORK

SUPPLEMENTARY MEDICAL REPORT—Confidential

Only for scientific purposes approved by the Board of Health, not open to inspection or subject to subpoena.

17c. Number born dead PREVIOUS to this pregnancy, including abortions
18a. †First day, last regular menstrual period (Month) (Day) (Year) — 18b. †Interval of menstrual cycle days
19. †Conditions present during this pregnancy (*Check one or more items*)

☐ Pre-eclampsia	☐ Nephritis	☐ German measles or other viral infection	☐ Benign or malignant neoplasms or related conditions. Specify.
☐ Eclampsia	☐ Heart disease	Specify disease and check trimester:	
☐ Hypertensive disease	☐ Diabetes	☐ 1st ☐ 2nd ☐ 3rd	☐ Other condition. Specify.
☐ Uterine bleeding not associated with labor	☐ Syphilis	☐ Injury or operation. Specify.	☐ None known.
☐ Pyelitis	☐ Tuberculosis		

20. Date of 1st prenatal visit — 21. Has mother's blood group been determined? — Result
22. Was serological test for syphilis done during THIS pregnancy or at delivery? — Date — Result
23. †Was induction attempted? — Indication
24. †Method of induction — Successful?
25. †Were manual, instrumental, or operative procedures used? — †Specify
26. †Indications for procedures
27. Indicate by X whether mother was private physician's patient ☐ general service patient ☐ — 28. Did delivery occur on ambulance service?
29. †Weight at birth grams or lbs. ounces. — 30. What was position at delivery?
31. †Duration of labor: 1st stage hours; 2nd stage hours mins.; 3rd stage mins.
32. Congenital abnormality? (Circle one): Questionable Yes No. — 33. Birth injury? (Circle one): Questionable Yes No.
34. Describe abnormality and/or injuries

†See definitions and instructions on inside front cover.

LABOR: Weight; Date 1st Visit; Blood Group; L. M. P. Mo. Yr. Cyc.; Sero. Test; Duration; Method of Induction
OPERATION: Name; Indication; Pos. at Del.; Indication for Induction; Complications

DO NOT WRITE IN THIS SPACE. MARGIN RESERVED FOR CODING AND BINDING

Registry of Births (*Continued*)

17c. Number born dead PREVIOUS to this pregnancy including abortions
18a. First day, last regular menstrual period (Month) (Day) (Year)
18b. Interval, menstrual cycle days
19. Conditions present during pregnancy
20. Date of 1st prenatal visit
21. Mother's blood group determined? (Yes) (No) Results
22. Serological test for syphilis? (Yes) (No) Date Result
23. Induction attempted? (Yes) (No) Indication
24. Method of induction Successful?
25. Operative, manual, or instrumental procedures used? (Yes) (No) Specify
26. Indications for procedures
27. Mother was private physician's patient ☐ general service patient ☐
28. Delivery on ambulance service?
29. Weight at birth lbs. and ozs. grams
30. Position at delivery
31. Duration of labor; 1st stage hrs.; 2nd stage hrs. mins.; 3rd stage mins.
32. Any congenital malformation?
33. Any birth injuries?
34. Describe

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Certificate of birth, used in New York City, showing, front, *above*, and back, *below*.

Results

Frequency of Inductions.—Of 165,150 live births in New York City in 1955, 7,694 (4.7%) were induced with intravenously given oxytocin. In 1956 the over-all reported incidence rose to 5.0%. In 1955, of 103,791 births on the private service, 6,890 (6.6%) were induced with oxytocin; of 58,991 births on ward services, 804 (1.4%) were induced. In 1956 an increase in utilization of oxytocin occurred in both private (7%) and ward services (1.7%). These data would indicate that oxytocin is used approximately five times more frequently on private than on ward services. A variation is noted among private patients, depending on whether they are delivered in voluntary or proprietary hospitals. Oxytocin is used two and one-half times more frequently on the private services of voluntary hospitals than on those of proprietary hospitals.

TABLE 1.—*Coding Methods Used for Data Taken from Birth and Fetal Death Certificates*

Code No.	Indications for Induction of Labor	Method of Induction of Labor
0	Not induced	Not induced
1	Elective	Other than oxytocin, successful
2	Therapeutic (including postmaturity, rupture of membranes, erythroblastosis, **Rh**—, premature separation of placenta, placenta previa, abruptio placentae, and ablatio placentae)	Other than oxytocin, not successful
3	Dead baby—no fetal heartbeat	Other than oxytocin, success not stated
4	Other (including nephritis, heart disease, diabetes, syphilis, tuberculosis, benign neoplasms, malignant neoplasms, and hypertension)	Posterior pituitary injection (Pituitrin) and/or oxytocin, successful
5	Uterine bleeding	Posterior pituitary injection and/or oxytocin, not successful
6	Toxemia (eclampsia and pre-eclampsia)	Posterior pituitary injection and/or oxytocin, success not stated
7	Indications not stated	Attempted induction, method not stated
8	Not stated whether induced	Not stated whether induced

Indications for Induction of Labor.—Elective induction constitutes approximately half of all inductions in 1955-1956. Of the 7,694 inductions in 1955, 3,688 were elective; of these, 3,548 (96%) were in private patients (table 2). Of the 6,890 inductions on the private service in 1955, 3,548 (51.5%) were for elective reasons, whereas of 804 on ward services, only 140 (17.4%) were elective. It would appear that on ward services oxytocin is used mainly where a therapeutic indication exists, whereas on private service the indication is chiefly elective. It is of interest that in 1956 an increased trend for elective induction is noted even on the ward services.

Use of Oxytocin by Type of Hospital.—Among the 100 hospitals (excluding two federal hospitals) with maternity services in New York City, three categories exist. They are (1) proprietary hospitals—privately owned and services limited entirely to private patients, (2) municipal hospitals—under the jurisdiction of the department of hospitals and limited to ward patients, and (3) voluntary hospitals—having both ward and private patients in varying proportions, depending on the given hospitals. A wide range in the use of intravenously given oxytocin was observed among the hospitals, in 1955, varying from a high of 29.9% to a low of 0.1% (table 3). In 1956 the hospital previously exhibiting the greatest use of this drug showed an even greater rise—to 54.2%.

Results of Questionnaire.—Oxytocin, for both induction and stimulation of labor, was used in 14.0% of 128,324 live births in 1955; 6.4% of live births were induced with intravenously given oxytocin, and 7.6% of live births occurred after its use for the acceleration of labor (table 4). The data obtained in 1956 showed little change from those of 1955. For both years combined, induction on the private service was recorded for 9.1% of the births as compared with 1.8% for the ward service. Stimulation on the private service was noted in 11.9% of cases as compared with 3.2% on the ward service. Induction was used almost twice as frequently on ward services of voluntary hospitals as on ward services of municipal hospitals. To a lesser degree the same trend is shown for stimulation. Among private patients, induction was used more than two and one-half times as frequently in voluntary hospitals as in proprietary hospitals. Again, to a lesser degree, the same trend is shown for stimulation.

Seasonal Variation.—Analysis of births after induction by oxytocin revealed a pattern of seasonal variation which was in marked contrast to that exhibited by all live births in New York City. Over

TABLE 2.—*Indications for Induction of Labor for Live Births, by Type of Service, New York City, 1955 and 1956*

	1955						1956					
	Total		Private Service		Ward Service		Total		Private Service		Ward Service	
Indication for Induction	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Elective	3,688	47.9	3,548	51.5	140	17.4	4,015	48.7	3,776	52.5	239	22.5
Therapeutic	1,910	24.8	1,702	24.7	208	25.9	1,721	20.9	1,525	21.2	196	18.5
No fetal heartbeat	1	0.0	1	0.0	...	...	...	...	...	...	...	...
Other	181	2.4	139	2.0	42	5.2	210	2.5	160	2.2	50	4.7
Uterine bleeding	82	1.1	58	0.9	24	3.0	94	1.1	79	1.1	15	1.4
Toxemia	602	7.8	443	6.4	159	19.8	472	5.7	331	4.6	141	13.3
Indications not stated	1,230	16.0	999	14.5	231	28.7	1,737	21.1	1,317	18.4	420	39.6
Total	7,694	100.0	6,890	100.0	804	100.0	8,249	100.0	7,188	100.0	1,061	100.0

a period of years no significant variation in number of births has been found to exist for New York City by month (table 5).

In 1955, peak months for births after induction were observed for July, August, and December. Similar peaks occurred (with the addition of June) in 1956. These rates were significantly higher than those prevailing during the remaining months. The rises were primarily a reflection of usage on private services. By contrast, on the ward service, where the indication is chiefly therapeutic, a plateau is noted. Significantly, in the elective group, the monthly peaks coincided with the over-all use on private service. It would appear that there is a relationship between peak periods of usage and vacation months (table 5).

TABLE 3.—*Percentage of Live Births Induced by Use of Oxytocin, by Type of Hospital, New York City, 1955, 1956*

Live Births Induced, %	1955				1956			
		Type of Hospital				Type of Hospital		
	Total	Voluntary	Proprietary	Municipal	Total	Voluntary	Proprietary	Municipal
0.1-1.0	16	6	4	6	14	5	2	7
1.1-2.0	21	10	6	5	12	3	5	4
2.1-3.0	10	5	4	1	12	7	5	..
3.1-4.0	12	5	6	1	7	2	5	..
4.1-5.0	9	5	4	..	12	8	4	..
5.1-6.0	10	9	1	..	8	6	2	..
6.1-7.0	2	2	..	..	5	4	..	1
7.1-8.0	2	2	..	..	6	6	..	..
8.1-9.0	4	4	..	..	6	5	..	1
9.1-10	3	3	..	..	1	1	..	..
10.1 & over	11	10	1	..	12	11	1	..
Total	100	61	26	13	95	58	24	13

Use of Oxytocin in Relation to Age and Parity of Mother.—In New York City, 34% of all live births are to primiparas and 32% to secundiparas. For live births occurring after oxytocin induction, the highest percentage is observed in the secundipara and next in the primipara. A significant observation was made that in 1956 there was an increased use of oxytocin for induction among mothers with a parity of three or more. The age distribution of the mothers in the group given oxytocin approximates the age distribution of mothers for all live births in New York City.

Conditions Present During Pregnancy.—On the live birth certificates for 1955 the check list indicated at least one or more conditions present during pregnancy in 8% of the cases. In the group of live births where oxytocin was used for induction, one or more conditions were checked in 15%. The higher frequency of "conditions" is as expected, since intravenously given oxytocin is administered for therapeutic as well as elective indications. Preeclampsia and eclampsia were leading conditions noted, with an incidence of 44.5% for both services combined; incidence in private service was 39.3% and in ward service 57.6% (table 6). The higher incidence of preeclampsia and eclampsia on the ward service is not unexpected. Hypertensive disease, heart disease, and neoplasms showed a higher incidence in patients on the private services than on the ward services.

Mode of Delivery.—In patients in whom induction by use of oxytocin was utilized, the percentage of spontaneous deliveries was significantly lower than in those not induced. Conversely, the percentage of forceps deliveries in the induced group was higher for both private and ward services than in those not induced. The higher percentage of forceps deliveries in those induced is to be expected, since oxytocin was used for the purpose of expediting delivery, for either elective or therapeutic reasons (table 7).

The percentage of breech deliveries induced by oxytocin on the private service was lower than that for the noninduced, whereas on the ward service the percentage of breech deliveries in the induced group was not significantly different from that of the noninduced. These differences observed are as anticipated, since in the private service induction is largely done for elective reasons and, therefore, a minimum of breech deliveries would be included.

On the private service, the percentage of cesarean sections in the induced group was much lower than in those not induced. For 1955, the incidence of cesarean section was 2.2% in the induced group as compared with 6.2% for those not so induced. In 1956 a similar relationship is noted (1.9% as com-

TABLE 4.—*Results on Questionnaire on Use of Oxytocin for Induction and Stimulation of Labor, New York City, 1955 and 1956*

Type of Hospital	Hospitals, No.	Live Births			Induction of Labor			Stimulation of Labor		
		Total	Private Service	Ward Service	Total	Private Service	Ward Service	Total	Private Service	Ward Service
1955										
Voluntary	49	78,327	54,836	23,491	6,895	6,444	451	7,681	6,933	748
Proprietary	16	20,806	20,806	...	833	833	...	1,383	1,383	...
Municipal	14	29,101	207	28,894	469	19	450	715	48	667
Total	79	128,324	75,939	52,385	8,197	7,296	901	9,779	8,364	1,415
1956										
Voluntary	51	81,270	57,539	23,731	6,648	6,025	623	9,582	8,502	1,080
Proprietary	18	24,667	24,661	6	1,134	1,122	12	1,942	1,917	25
Municipal	14	30,514	261	30,253	352	5	347	908	46	862
Total	83	136,451	82,461	53,990	8,134	7,152	982	12,432	10,465	1,967

pared with 6.1%). This finding also is as expected, since the indication for induction is primarily elective for private patients. By contrast, on the ward service, the percentage of cesarean section is higher in the induced group. This is another reflection of the relatively greater use of oxytocin for therapeutic indications among ward patients.

In 1955-1956, cesarean sections were performed on 372 patients who received oxytocin for induction. Seventy-eight percent of the sections (290) were performed on private patients. In 16.6% (62) of the 372 sections the indication for induction was stated as elective.

In analyzing the data on the group delivered by cesarean section after induction, there were 47 cesarean sections performed for fetal distress. Seven of these patients had received oxytocin on an elective basis. One may draw the inference that fetal distress followed the use of oxytocin, necessitating the section. Of the 98 sections performed for cephalopelvic disproportion, 23 were stated to have been induced electively. These were most likely unrecognized cases of disproportion. In 38 of the 98 cases of cephalopelvic disproportion, it was stated that induction had been used for therapeutic

TABLE 5.—*Live Births Induced by Oxytocin, by Month of Delivery and Type of Service, New York City*

Month of Delivery	Induced Deliveries, No.			Induced Deliveries, %			Elective Inductions	
	Total	Private Service	Ward Service	Total	Private Service	Ward Service	No.	%
1955								
January	476	422	54	3.8	3.4	1.2	159	1.2
February	521	461	60	4.2	3.8	1.3	199	1.6
March	558	487	71	3.9	3.2	1.4	227	1.6
April	637	567	70	4.7	6.3	1.5	287	2.1
May	637	580	57	4.5	6.2	1.2	289	2.0
June	658	607	51	4.7	6.8	1.0	337	2.4
July	726	655	71	5.4	7.7	1.5	302	2.6
August	792	719	73	5.6	8.4	1.3	418	3.0
September	605	527	78	4.4	6.1	1.5	317	2.3
October	639	565	74	4.7	6.6	1.5	309	2.2
November	668	586	82	5.0	6.9	1.7	355	2.7
December	777	714	63	5.8	8.2	1.3	429	3.2
Total	7,694	6,890	804	4.7	6.6	1.4	3,688	2.2
1956								
January	542	475	67	4.0	5.8	1.3	250	1.9
February	592	510	82	4.5	6.2	1.7	293	2.2
March	715	624	91	5.1	7.1	1.9	331	2.4
April	609	544	65	4.9	6.9	1.5	287	2.3
May	663	591	72	5.1	7.1	1.5	305	2.3
June	713	632	81	5.2	7.4	1.7	350	2.5
July	795	701	94	5.4	7.8	1.7	418	2.8
August	757	664	93	5.2	7.2	1.6	404	2.7
September	666	561	105	4.6	7.1	2.1	292	2.0
October	686	597	99	4.8	6.3	1.8	332	2.3
November	653	559	94	4.9	6.5	1.9	331	2.5
December	848	730	118	6.1	8.7	2.4	422	3.0
Total	8,249	7,188	1,061	5.0	7.0	1.7	4,015	2.4

reasons. In these cases it is difficult to reconcile the use of oxytocin in the face of recognized disproportion.

Seven mothers in this group had had previous cesarean sections. This raises the question as to why oxytocin was used at all in this group, since the risk of uterine rupture is acknowledged to be greater in such cases. Eight elderly primiparas (over 35 years of age) were subjected to induction before cesarean section.

Successful Use of Oxytocin.—A definition for successful does not appear in the instructions given for filling out birth certificates. It is understood as

TABLE 6.—*Conditions Present During Pregnancy for Live Births Induced by Oxytocin, by Type of Service, New York City, 1955*

Condition Present During Pregnancy	Induced Deliveries, No.			Induced Deliveries, %		
	Total	Private Service	Ward Service	Total	Private Service	Ward Service
Preeclampsia	495	320	175	43.1	38.6	54.5
Eclampsia	16	6	10	1.4	0.7	3.1
Hypertensive disease	97	75	22	8.5	9.1	6.9
Uterine bleeding not associated with labor	137	114	23	11.9	13.8	7.2
Pyelitis	23	17	6	2.0	2.1	1.9
Nephritis	12	9	3	1.0	1.1	0.9
Heart disease	43	37	6	3.7	4.5	1.9
Diabetes	40	19	21	3.5	2.3	6.5
Syphilis	8	6	2	0.7	0.7	0.6
Tuberculosis	11	5	6	1.0	0.6	1.9
Rubella or other viral infection	14	12	2	1.2	1.4	0.6
Injury or operation	22	21	1	1.9	2.5	0.3
Neoplasms	30	27	3	2.6	3.3	0.9
Other conditions	201	160	41	17.5	19.3	12.8
Total	1,149	828	321	100.0	100.0	100.0

meaning the induction of active labor resulting in birth per vaginam. Of the live births induced by use of oxytocin in 1955 and 1956, 80.6% were classified as successful, 2.8% unsuccessful, and 16.6% in neither category.

Among the 441 unsuccessful inductions, 222 (50%), of deliveries were by cesarean section. In this group 54 patients were given a trial of labor with use of oxytocin for a period of three hours or more. Twenty-six of these were in labor more than 12 hours before termination by cesarean section. It appears that a significant number exceeded a trial period of less than three hours. Of these 54 patients subjected to long trial periods of labor, 11 had received oxytocin electively.

Where "successful" was stated, 72 were delivered by cesarean section. This may indicate either an error in filling out the certificate or a misinterpretation of the term successful on the part of the doctor filling out the certificate (tables 8 and 9).

Premature Births Induced by Oxytocin.—For 1955-1956, more than 6% of all live births induced with oxytocin were premature as compared with 8.7% for all live births in New York City. On the ward services, the premature rate was 11.5%; however for those induced, the rate was higher (15.6%).

Of the 29,381 total premature live births in New York City for 1955-1956, 1,025 (3.5%) followed induction by oxytocin. Of these, 281 (27.4%) were the result of elective induction. Premature births associated with elective induction were highest in the months of June, July, August, and December. It is highly probable that labor was induced prematurely in these patients who might otherwise have gone to term (table 10).

Perinatal Mortality.—The perinatal mortality for 1955 in the induced private patients was 2.8%. For the remainder on the private services it was 2.2%. On the ward service the perinatal mortality was much higher for the induced group than for the rest (16.4% as compared with 3.8%). The much higher perinatal mortality on the ward services for the induced group may be due to the fact that oxytocin was used largely in cases in which there were complications such as toxemia, partial separation of the placenta, and other therapeutic indications.

TABLE 7.—*Live Births by Mode of Delivery and Service, New York City, 1955 and 1956*

	Induced Deliveries				Other Deliveries			
	Private Service		Ward Service		Private Service		Ward Service	
Mode of Delivery	No.	%	No.	%	No.	%	No.	%
1955								
Spontaneous delivery	2,928	42.5	427	53.1	50,892	52.5	39,429	67.8
Forceps	3,579	51.9	286	35.6	35,908	37.1	13,721	23.6
Breech	130	1.9	31	3.9	3,055	3.2	1,906	3.3
Cesarean section	155	2.2	35	4.4	5,985	6.2	2,183	3.8
Other	12	0.2	1	0.1	179	0.2	132	0.2
Not stated	86	1.3	24	2.9	876	0.8	822	1.3
Total	6,890	100.0	804	100.0	96,895	100.0	58,193	100.0
1956								
Spontaneous delivery	3,170	44.1	569	53.6	49,963	52.4	39,519	66.3
Forceps	3,650	50.8	383	36.1	35,472	37.2	14,299	24.0
Breech	153	2.1	32	3.0	3,066	3.2	1,969	3.3
Cesarean section	135	1.9	47	4.4	5,870	6.1	2,293	3.9
Other	9	0.1	4	0.4	182	0.2	147	0.2
Not stated	71	1.0	26	2.5	830	0.9	1,373	2.3
Total	7,188	100.0	1,061	100.0	95,383	100.0	59,600	100.0

The perinatal mortality for the spontaneous and forceps deliveries after induction (0.5 and 0.2%) is lower than for those not induced (2.8 and 1.3%). In these cases the use of oxytocin was limited to a highly favorable group where a low perinatal mortality generally prevails and where oxytocin was used largely for elective rather than for therapeutic reasons. (Perinatal mortality as herein calculated =[fetal deaths after 28 weeks gestation+infant deaths under 7 days]÷[fetal deaths after 28 weeks gestation+total live births]×1,000. Perinatal mortality data for 1958 are not available at the time of this report.)

The perinatal mortality for the induced deliveries on the private and ward services combined is higher than for the deliveries without induction. This difference is due entirely to the significantly higher perinatal mortality associated with breech deliveries and cesarean sections. For these two categories of breech and cesarean section it was observed that oxytocin was used predominantly for therapeutic indications. In a group of 206 breech deliveries where induction was used, there were 57 perinatal deaths with a perinatal rate of 27.7%. This rate is much higher than that found for breech deliveries where oxytocin was not used (16.6%). In a group of 201 cesarean sections where induction was attempted, there were 20 perinatal deaths with a perinatal rate of 10.0% as compared with a perinatal rate of 5.2% for cesarean sections where oxytocin was not used.

Puerperal Mortality.—In 1955-1956 there were 203 puerperal deaths reported; 103 fetuses were of 28 weeks' gestation or over. It is important to note that puerperal deaths have been encountered in reviewing hospital records where use of induction was not recorded on the birth or fetal death certificates, although oxytocin had been administered. Furthermore, an analysis limited to a study of deaths due to puerperal causes has its shortcomings in excluding patients who survived although they had developed serious complications after the administration of oxytocin. Several case reports are cited in which the administration of oxytocin for the induction of labor was believed to contribute to mortality.

CASE 1 (hypofibrinogenemia, amniotic fluid embolism).—A 23-year-old woman, gravida 3, para 2, blood type A, Rh+, was a private patient with an uneventful prenatal course. She was electively induced at term (40 weeks) with intravenously given oxytocin, 10 units per 1,000 cc. of 5% glucose solution. She had a rapid labor, proceeding from 1 cm. cervical dilatation to sudden precipitous delivery of a stillborn fetus, including the simultaneous delivery of the placenta, in the course of one hour and five minutes. The fetal heartbeat was stated to be normal until 10 minutes before delivery, after which time it was no longer heard. The delivery was followed by severe uterine hemorrhage with failure of the blood to clot. Visual examination of the cervix at this time revealed no evidence of laceration. The patient received 8 units of blood (4,000 cc.) and 10 Gm. of fibrinogen before good clotting resulted. This patient's blood pressure could be maintained at adequate levels only by the use of dilute intravenously given levarterenol (Levophed) bitartrate solution. A lower nephron nephrosis developed. This condition became progressively more severe, resulting in death six days after delivery. Postmortem examination revealed lower nephron nephrosis, pituitary necrosis, and pulmonary amniotic fluid embolism.

TABLE 8.—*Results in Induced Deliveries, by Mode of Delivery, New York City, 1955 and 1956*

	Induced Deliveries, 1955				Induced Deliveries, 1956			
Mode of Delivery	Total	Successful	Not Successful	Not Stated	Total	Successful	Not Successful	Not Stated
No operative procedure	3,355	2,731	50	574	3,739	3,066	49	624
Forceps deliveries	3,865	3,233	49	583	4,033	3,308	50	675
Breech deliveries	161	125	6	30	185	146	5	34
Version	10	10	...	...	13	8	...	5
Cesarean section	190	38	116	36	182	34	106	42
Other operative procedures	3	1	...	2	...	...	...	...
Mode not stated	110	84	6	20	97	69	4	24
Total	7,694	6,222	227	1,245	8,249	6,631	214	1,404
Percentage	100.0	80.9	3.0	16.1	100.0	80.4	2.6	17.0

Comment.—While it has been observed that, on occasion, when oxytocin has not been used, tumultuous rapid labor will result in a condition similar to that described above, it is definitely felt that the sequence of events in this fatal case were initiated by the use of oxytocin. Similar cases have been encountered in the course of review of hospital records in obstetric services over the past several years

where hypofibrinogenemia resulted after the use of intravenously given oxytocin for induction and/or stimulation of labor, particularly in toxemias of pregnancy. Many of these patients have survived with the administration of adequate fibrinogen and blood replacement. These cases have not been reported in the literature.

CASE 2 (ruptured uterus).—A 27-year-old woman, gravida 7, para 4, had an uneventful prenatal course with normal laboratory findings. She was admitted to the hospital at 34 weeks' gestation with ruptured membranes and mild uterine contractions. It was stated on the record that "because of desultory ineffectual contractions" oxytocin, 10 units per 1,000 cc. of 5% glucose solution, was administered by drip induction. The presentation in this case was left occipitotransverse. The cervix was soft, 50% effaced, and 2 cm. dilated. After three hours and 15 minutes of labor the patient spontaneously delivered a 2,268-Gm. (5-lb.) living infant and immediately went into severe shock. The patient received 10 units of blood, administered under pressure, and a hysterectomy was promptly performed. Examination revealed uterine rupture with massive retroperitoneal hemorrhage. The patient died on the operating room table.

Comment.—This patient had a premature infant with a gynecoid pelvis which was adequate. It is highly unlikely that this accident would have occurred spontaneously. Although the experienced obstetrician is aware that uterine rupture may occur spontaneously, particularly with increased parity, the risk of this complication is compounded by the use of a potent agent such as oxytocin.

CASE 3 (breach presentation, ruptured uterus).—A 21-year-old primipara with a breech presentation, left sacroanterior, was admitted to the hospital at term for elective induction of labor. The record noted an adequate gynecoid pelvis. After three and one-half hours of "good labor" after administration of oxytocin, the patient went into shock. On examination, the fetus was recognized to be in the upper abdomen and an immediate laparotomy was performed. Approximately 3,000 cc. of blood was found in the peritoneal cavity. A living 3,200-Gm. (7-lb.) male fetus was extracted from the peritoneal cavity. It was observed that the uterus was ruptured through the fundus. The patient received 14 units of blood, and the maintenance of her blood pressure was assisted by an intravenous solution of levarterenol. The patient then appeared in fair condition with a blood pressure of 110/86 mm. Hg and pulse rate 120 per minute. However, the urine output was diminished, and 12 hours postoperatively the patient's skin was cold and clammy. The hematocrit reading was 38%, blood pressure 100/70 mm. Hg, and blood platelet count 112,000 per cubic centimeter. Although the blood clotted and the prothrombin time was normal, the patient died 27 hours after operation due to massive retroperitoneal hemorrhage which was demonstrated at postmortem examination.

Comment.—This case illustrates the outcome of injudicious elective induction of labor with oxytocin in a primipara with a recognized breech presentation, resulting in a ruptured uterus.

Additional cases of ruptured uterus have been encountered in association with the use of intravenously given oxytocin for induction. Space does not permit the detailed accounts of at least 12 known cases of serious complications of ruptured uterus, severe hemorrhage with or without hypofibrinogenemia, and amniotic fluid embolism after the elective induction of labor with oxytocin. Most of these patients fortunately survived after prompt detection of the complication and immediate therapy. It is important to note that the above abstracted cases occurred on well-equipped obstetric services with qualified obstetricians.

Although all experienced, well-trained obstetricians are aware of the potential danger in the use of oxytocin, errors in judgment in the use of this drug and its occasional unpredictability will continue to add to the catastrophies presented.

Comment

For the years 1955 and 1956 oxytocin was used for the induction of labor in 4.9% of all deliveries in New York City, as reported on the birth certificates, and in 6.6%, as reported in the hospital questionnaire form. These figures are much higher than those reported by Hellman and co-workers [5a] in their analysis of 63,276 deliveries in 10 hospitals from 1951 through 1955 wherein it was stated that intravenously given oxytocin was used in 1.8% of the cases for the induction of labor. Elective induction accounted for 52% of all the oxytocin-induced deliveries on private services in New York City.

An outstanding finding which emerged from analysis of the data is the occurrence of peaks in the use of oxytocin in private patients for the induction of labor in the months of July, August, and December. This highlights the fact that it is extensively used for the convenience of the obstetrician and/or the patient. Various reports [6] from the literature indicate that convenience is a factor in the elective use of oxytocin for the induction of labor. Hellman states, "It seems highly improbable that these well trained and seasoned obstetricians would use a potentially dangerous drug to satisfy personal convenience." Willson,[7] in a study of 180 cases of

TABLE 9.—*Induced Deliveries Unsuccessfully Performed by Cesarean Section, by Indications for Induction of Labor and Duration of First Stage of Labor, New York City, 1955 and 1956*

Indications for Induction	1955							1956						
	Deliveries, Total	Duration of Labor, Hr.						Deliveries, Total	Duration of Labor, Hr.*					
		<3	3 to 12	12 to 24	>24	No Labor	Not Stated		<3	3 to 12	12 to 24	No Labor	Not Stated
Not induced	1	...	...	1	...	...	...	...	...	...	...	...	...
Elective	21	...	4	2	2	13	...	14	...	...	3	10	1
Therapeutic	38	3	6	4	3	20	2	37	2	5	3	25	2
Other	9	...	1	...	...	8	...	6	...	...	1	5	...
Uterine bleeding	1	...	...	...	...	1	...	5	...	1	...	4	...
Toxemia	28	...	3	...	...	23	2	30	...	3	2	25	...
Indications not stated	18	...	3	3	1	11	...	14	...	2	1	10	1
Total	116	3	17	10	6	76	4	106	2	11	10	79	4

* In no case did labor continue for more than 24 hours.

Comment

For the years 1955 and 1956 oxytocin was used for the induction of labor in 4.9% of all deliveries in New York City, as reported on the birth certificates, and in 6.6%, as reported in the hospital questionnaire form. These figures are much higher than those reported by Hellman and co-workers [5a] in their analysis of 63,276 deliveries in 10 hospitals from 1951 through 1955 wherein it was stated that intravenously given oxytocin was used in 1.8% of the cases for the induction of labor. Elective induction accounted for 52% of all the oxytocin-induced deliveries on private services in New York City.

An outstanding finding which emerged from analysis of the data is the occurrence of peaks in the use of oxytocin in private patients for the induction of labor in the months of July, August, and December. This highlights the fact that it is extensively used for the convenience of the obstetrician and/or the patient. Various reports [6] from the literature indicate that convenience is a factor in the elective use of oxytocin for the induction of labor. Hellman states, "It seems highly improbable that these well trained and seasoned obstetricians would use a potentially dangerous drug to satisfy personal convenience." Willson,[7] in a study of 180 cases of

elective induction with intravenously given oxytocin, concludes that its use is seldom justified in normal pregnancy.

The following factors are related to the use of oxytocin.

Ruptured Uterus.—It would appear that, in the puerperal deaths herein described, the use of oxytocin led to rupture of the uterus. Case reports corroborate the sequence of ruptured uterus occurring after elective use of oxytocin.[8]

Uterine Hemorrhage.—Within the limitations of the data obtained from certificates, the problem of postpartum or intrapartum hemorrhage is not ascertainable except as associated with a puerperal death. Sotto and Wildhack [9] indicate a higher proportion of severe hemorrhages after the elective use of oxytocin. The question of hypofibrinogenemia has been raised and is suggested in our review of puerperal deaths.

TABLE 10.—*Premature Live Births, Induced by Oxytocin, by Month of Delivery, New York City, 1955 and 1956*

Month of Delivery	Induced Deliveries, 1955				Induced Deliveries, 1956			
	Total		Elective		Total		Elective	
	No.	%	No.	%	No.	%	No.	%
January	27	5.7	4	0.8	53	9.8	11	2.0
February	27	5.2	1	0.2	42	7.1	12	2.0
March	39	7.0	11	2.0	44	6.2	11	1.5
April	48	7.5	10	1.6	40	6.6	6	1.0
May	40	6.3	17	2.7	41	6.2	8	1.2
June	43	6.5	13	2.0	47	6.6	16	2.2
July	47	6.5	17	2.3	42	5.3	16	2.0
August	51	6.4	24	3.0	40	5.3	12	1.6
September	48	7.9	12	2.0	42	6.3	7	1.1
October	28	4.4	4	0.6	40	5.7	9	1.3
November	45	6.7	17	2.5	33	5.1	9	1.4
December	64	8.2	18	2.3	54	6.4	16	1.9
Total	507	6.6	148	1.9	518	6.3	133	1.6

Perinatal Mortality.—Much more information needs to be added to our findings, which suggest that in cesarean section and breech deliveries the prior use of oxytocin appears to increase mortality. Several reasons may be postulated for this:

1. Where oxytocin was given intravenously, an indicated cesarean section was possibly delayed, resulting in fetal distress. 2. In patients with borderline pelvic measurements, a trial of labor may be unduly prolonged when oxytocin is used and result in fetal damage. This is in agreement with the views expressed by Cosgrove and Weaver.[10] 3. The use of oxytocin may result in fetal distress by causing prolonged uterine contraction or tumultuous labor.

On the other hand, although mortality in the case of spontaneous delivery after use of oxytocin is not increased, a matched control group is needed to compare induced spontaneous deliveries with those not induced, where the same socioeconomic factors and level of obstetric care prevail.

Fetal Distress.—Trauma to the infant, short of being fatal, is not ascertainable from certificate data. Seven cases of fetal distress after the elective use of oxytocin which necessitated cesarean section have been mentioned above. This would substantiate the belief that occasionally the fetus is subjected to needless damage. Long-term follow-up of such individuals would be of invaluable help.

Many of the questions raised here regarding the use of intravenously given oxytocin and its effect on the mother and upon the infant remain unanswered. It is hoped that this study will stimulate further investigations on the use of oxytocin for acceleration and/or induction of labor.

Summary

An analysis has been made of the use of intravenously given oxytocin (Pitocin) in New York City for 1955-1956, as ascertained by birth and fetal death certificates and by questionnaire. Oxytocin was used for induction in 4.8% of all live births, as determined from certificate data. Induction of labor with intravenously given oxytocin occurred primarily on the private services of the voluntary hospitals. Of all elective inductions, 95.1% occurred on private services. Labor was induced by use of oxytocin almost five times more frequently in the private patients than in the ward patients.

A geographical variation was noted in the frequency of use of oxytocin for the induction of labor. Of the five boroughs in New York City, Brooklyn was recorded as having the highest incidence. A marked seasonal variation in the use of oxytocin was observed on the private services. The peak months were July, August, and December. Elective induction was chiefly responsible for the seasonal variation observed. No such variation occurred on the ward services.

Of the 1,025 premature infants born after the use of oxytocin, 281 (27.4%) were born after elective induction. The highest incidence of premature births after elective induction occurred in June, July, August, and December. The infant mortality rate was almost twice as high for infants delivered by cesarean section where oxytocin had been previously used as compared with those delivered by cesarean section where previous induction had not been attempted. In several cases of puerperal mortality oxytocin appeared to have initiated an unfortunate sequence leading to rupture of the uterus, hypofibrinogenemia, and uterine hemorrhage.

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References

1. Page, E. W.: Response of Human Pregnant Uterus to Pitocin Tannate in Oil, Proc. Soc. Exper. Biol. & Med. **52**:195-197 (March) 1943.

2. Theobald, G. W., and others: Use of Posterior Pituitary Extract in Physiological Amounts in Obstetrics: Preliminary Report, Brit. M. J. **2**:123-127 (July 17) 1948.

3. Hellman, L. M.: Factors Influencing Successful Posterior Pituitary Treatment of Functional Uterine Dystocia

with Particular Consideration of Its Intravenous Administration, Am. J. Obst. & Gynec. **57**:364-369 (Feb.) 1949.

4. Engstrom, L., and Ohlson, L.: Value of Intravenous Oxytocin Drip in Obstetric Cases, Acta obst. et gynec. scandinav. **35**:414-424, 1956. Faris, I. B., and Kahlenberg, B.: Intravenous Pitocin by Drip Method in Induction of Labor, J. Obst. & Gynaec. Brit. Emp. **61**:96-102 (Feb.) 1954. Ferguson, J. H., and Slate, T. A.: Induction of Labor by Dilute Pitocin Infusion, South. Surgeon **16**:1106-1114 (Nov.) 1950. Gold, P. M., and Angell, J. H.: Elective Induction of Labor Using Oxytocin Injection Intravenously, U. S. Armed Forces M. J. **4**:555-557 (April) 1953. Gordon, C. A.: Intravenous Use of Dilute Posterior Pituitary Extract During Labor, Am. J. Surg. **82**:76-80 (July) 1951. Hellman, L. M.; Harris, J. S.; and Reynolds, S. R. M.: Intravenous Pituitary Extract in Labor with Data on Pattern of Uterine Contractility, Am. J. Obst. & Gynec. **39**:41-48 (Jan.) 1950. Theobald, G. W.; Kelsey, H. A.; and Muirhead, J. M. B.: Pitocin Drip, J. Obst. & Gynaec. Brit. Emp. **63**:641-662 (Oct.) 1956.

5. (*a*) Hellman, L. M.; Kohl, S. G.; and Schechter, H. R.: Pitocin—1955, Am. J. Obst. & Gynec. **73**:507-517 (March) 1957. (*b*) Page, E. W.: Usefulness of Intravenous Pitocin Infusions in Obstetrics, West. J. Surg. **62**:125-138 (March) 1954.

6. Ratzan, W. J., and Shulman, A.: Intravenous Pitocin and Elective Induction of Labor, Obst. & Gynec. **6**:493-498 (Nov.) 1955. Bishop, E. H.: Elective Induction of Labor, Obst. & Gynec. **5**:519-527 (April) 1955.

7. Willson, J. R.: Elective Induction of Labor: Is It Justifiable in Normally Pregnant Women? Am. J. Obst. & Gynec. **65**:848-858 (April) 1953.

8. Guttmacher, A. F., in discussion on Keettel, W. C.; Randall, J. H.; and Donnelly, M. M.: Hazards of Elective Induction, Am. J. Obst. & Gynec. **75**:505 (March) 1958.

9. Sotto, L. S., and Wildhack, R. H.: Elective Induction of Labor, Am. J. Obst. & Gynec. **75**:28-35 (Jan.) 1958.

10. Cosgrove, R. A., and Weaver, O. S.: Analysis of 1,000 Consecutive Midforceps Operations, Am. J. Obst. & Gynec. **73**:556-568 (March) 1957.

PREVENTION OF INFECTION OF URINARY TRACT IN PRESENCE OF INDWELLING CATHETERS

DESCRIPTION OF ELECTROMECHANICAL VALVE TO PROVIDE INTERMITTENT DRAINAGE OF THE BLADDER

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Catheters kept in the urinary bladder as long as four days provoke bacteriuria in almost every case. The technique here described prevents this complication by continuous irrigation with 0.25% acetic acid through a catheter with three lumens. One passage permits distention of the retaining balloon; the other two passages are for inflow and outflow. The method was successful in more than 100 patients. The rate of inflow of the acetic acid solution was roughly equal to that of urine production, but it was adjusted so that the effluent was kept at pH 5.0 or less and the bacterial count at less than 1 million per milliliter. Outflow was interrupted periodically by use of an electromechanical valve to permit filling of the bladder and avoid prolonged contraction. In some patients it was possible to leave the catheter in situ as long as 60 days without inducing bacteriuria.

When an indwelling catheter has been in the bladder for 24 hours, the incidence of bacteriuria in patients whose urines were previously sterile is about 50%. After four days of constant catheterization 98-100% of patients develop 100,000 or more bacteria per milliliter of urine.[1] The hazards of catheterization have been widely recognized and the medical profession has been cautioned against the indiscriminate use of indwelling catheters.[2] On the other hand, the indwelling catheter is often indispensable to the management of many clinical conditions. The desirability of using the indwelling catheter without inducing bacteriuria is manifest.

The bacteriuria that follows the use of indwelling catheters is due to the constant entry of bacteria into the bladder when the catheter is in place. The probable route of entry of the bacteria is the film of exudate that forms in the urethra in response to the presence of the catheter.[3] This film is an excellent culture medium for bacteria and links the fecal

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flora of the perineum with the interior of the bladder. It is not surprising, therefore, that the prophylactic use of chemotherapeutic and antibiotic agents has not reduced the incidence of bacteriuria significantly. The perineal and fecal flora contain bacteria that are resistant or may become resistant to commonly used antibacterial agents. Therefore, the net effect of specific antibacterial prophylaxis is to convert a drug-sensitive flora to a resistant one.[2b]

The prevention of infections due to indwelling catheters depends upon either preventing the entry of bacteria into the bladder or removing bacteria from the bladder promptly after entry. Prevention of entry has not yet been achieved, although it is reasonable to suppose that proper choice of the diameter of a catheter and careful technique in insertion may delay the entry of bacteria. Cleansing the bladder of bacteria promptly after they have entered it can be achieved if the bladder is rinsed with an antibacterial solution so that bacterial multiplication cannot occur. If antibacterial solutions are to be useful for such a purpose, they should be nontoxic, relatively inexpensive, active against all of the bacterial species that may be found in the bladder, and unlikely to permit resistant strains to emerge.

Acetic Acid as Bacteriostatic Agent

Acetic acid satisfies these conditions. It is a potent bacteriostatic agent. At pH 5.0, which is not lethal for most pathogens of the urinary tract, as little as 0.01 M (0.06%) acetic acid will sterilize a broth culture of Escherichia coli. None of the urinary tract pathogens so far tested has resisted 0.02 M acetic acid at pH 5.0. The antibacterial action of organic acids has been known for many years, and acetic acid has been a standard rinsing solution in douches and bladder rinses. Its limitations have been few, but they are critical. Chief among these is that the antibacterial action of acetic acid is apparently linked to the number of unionized molecules in solution; if the pH is permitted to rise, the antibacterial action falls off sharply. Furthermore, the antibacterial action of acetic acid requires prolonged contact between the acid and the bacteria, so that more or less continuous presence of acetic acid in the bladder must be maintained.

The simplest means for providing continuous administration of acetic acid is by the use of an ordinary double-lumen indwelling catheter. This type of catheter actually has three lumens: one for distending the retaining balloon and two running from the interior of the bladder. A solution of 0.25% acetic acid (prepared by adding 2.5 ml. of glacial acetic acid to 1 liter of sterile water) drips into one of these tubes, and the mixture of acid and urine leaves through the other. The rate of flow of the acid is adjusted so that the effluent is kept at pH 5.0 or less and the bacterial count at less than 100,000 bacteria per milliliter of urine. The pH can be tested by inserting a strip of pH paper, such as nitrazine paper, into the effluent. The bacterial count is determined by microscopic examination of a stained drop of uncentrifuged effluent. If no bacteria are seen, the bacterial count is generally less than 100,000 per milliliter.[1] The bacterial count can be determined more precisely by standard pour plate colony counts of serial dilutions of the effluent. Only rarely, if adequate amounts of acetic acid are used, will any bacteria be found in the culture.

The procedure outlined above is highly effective if the flow of acetic acid is sufficiently rapid. Ordinarily a flow of 0.25% acetic acid equal to the rate of urine flow is adequate. When a highly alkaline urine is encountered, as in Proteus infections, the rate of flow may be increased. If necessary, a higher concentration of acetic acid, such as 0.5%, may be used. In extremely difficult situations, in which the urine has remained alkaline despite rinsing of the bladder with acetic acid, a stronger acid, such as 0.25% lactic acid, may be used to acidify the urine to pH 5.0 or less. Acetic acid may then be substituted for lactic acid, since on a molar basis acetic acid is about 10 times as active as lactic acid as a bacteriostatic agent at pH 5.0.

Drainage System for Bladder

The continuous drainage system just described will maintain the bladder free of bacteria if properly managed. However, after two or three days, the bladder may become so contracted that when the catheter is removed the patient will often complain of frequency and marked pelvic discomfort, because of the small volume of the bladder. The effects of contraction of the bladder may be circumvented by providing intermittent filling of the bladder to a physiological volume. This may be done effectively by the use of tidal drainage, which supplies both a physiological stimulus and a constant supply of antibacterial fluid to the bladder. Unfortunately, tidal drainage requires an apparatus that is sufficiently complex to have aroused substantial resistance from house staff and nursing staff alike. Some simplification of this approach is desirable. In addition, tidal drainage often will not work in individuals with hypotonic or irritable bladders.

The two-way catheter drainage system that has been described may be modified to permit the bladder to increase its volume. Initially, the effluent tube was clamped and released for only five minutes

every hour, permitting accumulation and periodic discharge of the contents of the bladder. In this manner, the bladder could be distended to hold a volume of several hundred milliliters, depending upon the rates of flow of urine and of acetic acid into the bladder. However, the personnel problems involved in the manual control of the clamp were such that it seemed desirable to have this task performed electromechanically.

Electromechanical Device

An electromechanical device for controlling the discharge of fluid from the bladder is shown in the figure. It consists of a motor-driven timer, which actuates a solenoid-operated clamp. The effluent tube is placed within the clamp, which is in the open position when no electrical current is flowing. When the switch is turned on, the clamp shuts and no release of fluid from the bladder can occur. The timer opens the clamp at periodic intervals. The present apparatus, which is the result of testing of several alternatives, provides four timing cycles. The clamp may be kept closed for 55 minutes and opened for 5 minutes, or it may be closed for 25 minutes and opened for 5 or closed for 15 minutes and opened for 15. The device can be hooked to the bedrail or bedspring, is virtually noiseless, and is "fail safe" (any mechanical or electrical failure causes the clamp to open automatically).

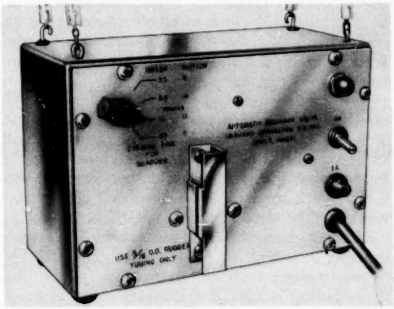
The apparatus has been used in more than 100 patients who have required indwelling catheters. Less than 10% of patients whose catheters have been managed by this method have developed bacteriuria, whereas 100% of patients given saline instead of acetic acid have developed bacteriuria.[4] Patients with indwelling catheters have been maintained for as long as 60 days by this procedure without any bacteria being found in the bladder.

In practice, one lumen of the indwelling catheter is attached to a bottle fitted with a dropping device and containing 0.25% acetic acid. The rate of flow into the bladder is controlled by an ordinary tubing clamp. The effluent from the bladder is collected in a receptacle beneath the bed. The rubber tubing passing from the catheter to the collecting bottle is placed in the clamp of the electromechanical valve. For most purposes the cycle is kept at 55 minutes closed and 5 minutes open. If the capacity of the bladder is small, a shorter cycle may be used. The 15-minute cycle has been particularly useful in the management of pyelostomies and in dealing with indwelling catheters in small children.

No important difficulties have arisen thus far in the use of this device. The clinical results, which will be the subject of a more detailed report elsewhere, have indicated that the acid rinse as presently used induces microscopic hematuria in about 5% of patients. About 1% develop pelvic distress and gross hematuria. Further improvements in the nature of the antibacterial rinsing fluid are expected to diminish the incidence of these local reactions.

Summary

In order to avoid infection of the urinary tract during indwelling catheterization, the bladder should be rinsed constantly with an antibacterial solution. Dilute acetic acid (0.25%) is an adequate solution if its flow is sufficiently rapid to provide a pH of less than 5.0 and bacterial counts in the urine of less than 100,000 bacteria per milliliter. The acetic acid rinse is conveniently administered through one lumen of a two-way catheter and the acidified urine is discharged through the other. An electromechanical valve may be used for providing intermittent drainage of the bladder simply and reliably.



Electromechanical device for controlling discharge of fluid from bladder.

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This study was aided by grants from the National Institutes of Health, U. S. Public Health Service, and the Massachusetts Heart Association.

References

1. Kass, E. H.: Asymptomatic Infections of Urinary Tract, Tr. A. Am. Physicians **69:**56-64, 1956; Bacteriuria and Diagnosis of Infections of Urinary Tract with Observations on Use of Methionine as Urinary Antiseptic, A. M. A. Arch. Int. Med. **100:**709-714 (Nov.) 1957.

2. (*a*) Beeson, P. B.: Case Against Catheter, editorial, Am. J. Med. **24:**1-3 (Jan.) 1958. (*b*) Kass, E. H.: Symposium on Newer Aspects of Antibiotics: Chemotherapeutic and Antibiotic Drugs in Management of Infections of Urinary Tract, Am. J. Med. **18:**764-781 (May) 1955.

3. Kass, E. H., and Schneiderman, L. J.: Entry of Bacteria into Urinary Tracts of Patients with Inlying Catheters, New England J. Med. **256:**556-557 (March 21) 1957.

4. Kass, E. H.; Dandrow, R. V.; and Norton, J. C.: To be published.

AMNESIA-ANALGESIA FOR THE MANAGEMENT OF CHILDREN TOO YOUNG TO COOPERATE

FURTHER OBSERVATIONS

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Cardiac catheterization, like many other diagnostic and therapeutic procedures, poses especially difficult problems for the anesthesiologist when the patient is too young to cooperate. The procedure here outlined consists of a sequence of steps whereby the requisite degree of tranquility, analgesia, and amnesia can be attained without interfering with the tests or examinations being carried out. Upon this background it is possible to superpose anesthesia with nitrous oxide, cyclopropane, or ether for short periods when necessary. Exact calculation of dosages is essential. Applied in 133 cases of cardiac catheterization and 100 comparable operations of other kinds, this plan has reduced to a minimum the respiratory and other reflex disturbances which otherwise make it difficult to interpret results.

Some months ago I [1] reported the results of application of a procedure which my colleagues at the Mayo Clinic in 1957 asked me to develop for the management of cardiac catheterization in children too young to cooperate. In that report I based my observations on experience with 36 children, 9 months to 12 years old, who had cardiac defects and defects of the great vessels. Fifty-one other children were managed by the same procedure, plus the use of anesthesia with nitrous oxide, oxygen, and ether, preparatory to tonsillectomy and adenoidectomy or operations on the eye. My series now includes 133 children who underwent cardiac catheterization and 100 who underwent other operations which demand a degree of tranquility and cooperation from the patient.

It is emphasized again that the procedure in question does not consist primarily of anesthesia alone. Rather, it is a special application of both analgesia and amnesia. The important aspect is the fact that the agents used do not interfere with the test or examination being carried out, as they would if they were primarily anesthetic agents administered, particularly by inhalation. The patient breathes either air or oxygen throughout the test or examination, so that it is possible for the physician during cardiac catheterization, for instance, to interpret physical data readily, to carry out Van Slyke tests, and to reach an unimpeded decision as to the lesion or lesions present, provided that technical difficulties arising during the course of the test do not complicate matters unduly.

Method

The mechanics of the procedure are set forth in the table. First of all, the pediatrician furnishes an estimate of the degree of risk of cardiac catheterization, based on a scale of 1 to 4 in which 4 is the gravest risk. Next, the parents or relatives of the child are told specifically what is to be done and what the risk is. Then I weigh the child myself. This is of prime importance, since experience has shown that in some instances only estimates of body weight will be furnished by the referring physicians. Catheterization of the heart then proceeds, after which I receive the child into my care, where he remains until I send him to the hospital or until the parents or relatives take him home.

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The three factors are the weight of the child, the passage of time checked carefully by the clock, and abatement of the movements of the child. The chief hazard in this method involves exact measurement of the dose of the drug from the container in which the manufacturer supplies it. The smaller the child, the more difficult it is to measure exactly the required dose. Only recently have I been able to obtain a mixture of levorphanol (Levo-Dromoran) tartrate and levallorphan (Lorfan) tartrate compounded in such a manner as to assure me that 0.2 cc. per 10 lb. of body weight of the child is the correct dose. I also have been able to obtain promethazine (Phenergan) hydrochloride in a correspondingly correct dilution and alphaprodine (Nisentil) hydrochloride and proheptazine (Wy 757) as well. Each time the formula has been modified, the results have been unsatisfactory from the standpoint of both the management here described and the test itself.

To calculate the dose of thiopental (Pentothal) sodium to be administered rectally, the actual weight of the child in pounds is used. To calculate the dose of drugs to be administered by injection, the weight in pounds generally is lowered to the next even number in units of 10 or to make the figure in units of 10 or halfway between. That is,

if a child weighs 41 lb., the weight employed in the calculation would be 40 lb. If the weight were 46 lb. the figure 45 would be used for calculation of the dose, or if the weight were 49 lb. the figure 50 might be used. Any arbitrary increase in the weight for purposes of calculation of the dose can be used only when the patient is relatively robust.

Some children do not, because of intrinsic physiological factors or deficiencies of which we are not yet aware, tolerate the procedure well, and tion has been seen to exert an adverse effect on the circulation. Heavy crying on the part of a child also is a sign of impending difficulties with the circulation. A child who is in a very unsatisfactory state of debilitation obviously is not an ideal candidate for the method.

The blood pressure of three children who manifested these signs decreased precipitately to 22, 28, and 98 mm. Hg; one died 12 hours after cardiac catheterization, one died 15 hours after the pro-

OUTLINE—MAY BE HAZARDOUS IF NOT FOLLOWED EXACTLY

NOTE: BEFORE CATHETERIZATION, THE ANESTHESIOLOGIST HIMSELF SHOULD WEIGH THE PATIENT AND EXPLAIN TO THE RELATIVES WHAT IS TO BE DONE. IN THE COURSE OF CATHETERIZATION, HE SHOULD GO OUT AND REASSURE THE RELATIVES NOW AND THEN.

Procedure:

	Step	Agent*	Dose: Mg.	Dose: Relation to Body Wt.	Route	Remarks
Preoperative	1	thiopental (Pentothal) sodium	15	per 1 lb.	rectal	
	2	Wait 5 to 10 min. for thiopental sodium to take such effect that patient will not remember IM injections of step 3				
	3	Step 3 consists of injection, at one time, of 4 drugs, all mixed together in one syringe, as follows (a, b, c, d):				
	a	levorphan (Levo-Dromoran) tartrate	0.2 WARNING see remarks	per 10 lb.	IM	Even if a child weighs more than 100 lb., if he is 10 yr. of age or less, dose of levorphan MUST NOT EXCEED 1 mg. Give NO additional levorphan for same procedure
	b	levallorphan (Lorfan) tartrate	0.1	per 10 lb.		Mixture given in step 3 is not clear. Do not be alarmed by milky appearance. It can be used without being cleared. However, it can be cleared by mixing with 1 cc. of 1% procaine hydrochloride
	c	promethazine (Phenergan) hydrochloride	2.0	per 10 lb.		
	d	proheptazine (Wy 757) or alphaprodine (Nisentil) hydrochloride	1.0	per 10 lb.		
	4	Wait 20 min. for analgesia, prospect of amnesia, or both to develop				
	5	Infiltrate with local anesthetic line of incision for venostomy				
	6	proheptazine or alphaprodine	1.0	per 10 lb.	IM	This step is necessary IF CHILD IS RESTLESS, as most children are
Operative	7	Wait 5 min. in expectation that child will become sufficiently quiet to permit initiation of cardiac catheterization and will remain quiet for 1 to 2 hr. If child is not sufficiently quiet for cardiac catheterization to start, or if catheterization is in progress and child becomes unduly restless, give following:				
	a	proheptazine or alphaprodine	1.0	per 10 lb.	IM	Dose may be given again at intervals of 45 min. to allay restlessness
	b	If patient moves within 1¾ to 2 hr. after the first enema of thiopental (see step 1), and if the procedure is expected to take 3 to 5 hr. (NOT if procedure is expected to be short: i. e., 2-3 hr.) repeat step 1 and, if necessary to keep patient quiet, step 7a.				
Postoperative	8	After catheter tip has been removed from heart, but before it has been removed from vein, give following drugs:				
		bemegride (Megimide; 3-ethyl-3-methylglutarimide) and amiphenazole (Daptazole)	10 ABSOLUTE 30†	WITHOUT RELATION TO BODY WEIGHT	via catheter	Five min. after this dose is given, if necessary to arouse patient, same dose, BUT GIVEN INTRAMUSCULARLY, may be used once again
	9	Now, because of congenital cardiac defect and stress of procedure, begins a period that may be HAZARDOUS. Usually, about 1 min. after bemegride is given, patient will arouse sufficiently to answer questions. Thereafter, for 1 to 2 hr., he should be in state much resembling normal light sleep, from which he can be easily aroused. BUT if BLOOD PRESSURE FALLS and CYANOSIS develops, give following:				
	a	oxygen			inhalation	Five min. after this dose, if necessary to raise blood pressure more and to produce signs of arousal, same dose by same route may be given once again. Then, if respiration is not good, give 0.1 mg. of levallorphan intravenously
	b	mephentermine (Wyamine) sulfate or methylphenidate (Ritalin) hydrochloride	7.5 ABSOLUTE 7.5 ABSOLUTE	WITHOUT RELATION TO BODY WEIGHT	IM	

*Until the manufacturers concerned offer the following agents in the precise quantities required for the procedure in question, I use the following proportions:

levorphan	1.0 mg.
levallorphan	0.5 mg.
alphaprodine	5.0 mg.

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

proheptazine or alphaprodine	5.0 mg. (steps 6 and 7a)

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

promethazine	10.0 mg.

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

†If child weighs less than 50 lb., dose of amiphenazole may be reduced to 15 mg.

OUTLINE—MAY BE HAZARDOUS IF NOT FOLLOWED EXACTLY

difficulties will arise when such patients are managed by the method described. Some vomit once or twice after they awaken, and this applies to those who have not undergone cardiac catheterization as well as to those who have, indicating that the vomiting may not be referable to the heart. Some of the premonitory signs are known. A child who holds his breath probably will not adapt himself satisfactorily to the procedure, for such an accedure, and one died immediately after the procedure. Studies are under way to elicit additional causative factors in such difficulties.

Following is an illustration of a difficulty that can arise. One of the assistants, without consultation, decided to administer a small quantity of thiopental sodium intravenously through the cardiac catheter. The result was a sudden depression, with a decrease in blood pressure which is entirely

unsatisfactory as far as the test is concerned. Moreover, such an action is quite unsatisfactory to me, since I have no way to control the dose administered. Therefore, further intravenous injections have been disallowed. If the child is too active, thiopental sodium is administered again by rectum.

One of the questions that has been answered more or less since the preliminary report [2] has to do with the fact that about 10% of these children are resistant to the action of the thiopental sodium enema and the hypodermic injection. It now appears certain that, if the child is still crying and moving 15 minutes after the first rectal administration of thiopental sodium and also 10 minutes after the hypodermic injection, a second full dose of thiopental sodium should be administered rectally. In only one instance in this series was the child sufficiently unconscious that five minutes after the rectal administration of thiopental sodium the child appeared to have an overdosage. In this case nothing further was used in a procedure that lasted two and one-half hours. This emphasizes the importance of the body movements of the child.

A possible criticism of this method might be that it causes the patient to sleep for two or three hours after the test has been completed. However, such an effect is not hazardous, and, if it constitutes a deficiency, the disadvantage is more than outweighed by the enhanced safety which the method provides.

I may point out that in this series I have had only two or three patients who were relatively overweight. Most of the patients have been underweight, and this may explain why the method has been so satisfactory. Nevertheless, even when the patient is overweight I am convinced that the statement, "Even if the child weighs more than 100 lb., if he is 10 years of age or less, the dose of levorphan must not exceed 1 mg.," is correct and should be observed scrupulously.

Applications Other Than in Cardiac Catheterization

This method also has been applied in almost 100 procedures other than cardiac catheterization. Irradiation therapy for retinoblastomas of the eye, heretofore a difficult anesthesia-analgesia-amnesia problem, is well suited to the technique I have described. There are three phases of this problem: (1) an initial period of surgical anesthesia of moderate length for implantation of seeds or needles, (2) an intermediate period of amnesia-analgesia extending several hours, during which the implant must not be disturbed, and (3) another period of surgical anesthesia of relatively short duration for the removal of the seeds or needles.

Thiopental sodium is administered rectally to the child on a basis of 15 mg. per pound of body weight. When a light sleep is evident, these agents are administered intramuscularly: 0.2 mg. of levorphanol, 0.1 mg. of levallorphan, 0.1 mg. of alphaprodine, and 2.0 mg. of promethazine, each per 10 lb. of body weight. This is an exacting technique: reference should be made to the accompanying table for the details. Venipuncture can be done with ease at this point, preferably with a plastic needle, so that fluids may be given continuously.

The patient is then anesthetized by gradually increasing the concentration of ether in an oxygen (3 liters) and nitrous-oxide (7 liters) mixture until a depth of anesthesia appropriate for intubation is obtained, at which time an endotracheal tube is passed orally. Surgical anesthesia is maintained while the radon seeds are implanted. After this, maintenance of inhalation anesthesia is discontinued and the endotracheal tube is removed. The child will then remain in a state of amnesia-analgesia for several hours without disturbance of the implanted radon or radium.

When radon or radium is to be removed, the patient again is anesthetized. Since this is a relatively short procedure, cyclopropane is the anesthetic agent of choice and endotracheal intubation usually does not appear justified. The recommended initial mixture is 6 liters of nitrous oxide, 3 liters of oxygen, and 1.5 liters of cyclopropane, administered by mask. When a surgical depth of anesthesia is reached, a tube is introduced into the nostril, away from the surgical field, and the other nostril and the oral airway are occluded. Inhalation anesthesia is maintained through the nasal tube, and the mixture of cyclopropane is adjusted to that minimal concentration which will be adequate for anesthesia. At cessation of the operation ventilation is begun by the administration of 100% oxygen. The child will arouse quickly but will lapse into a light sleep if left undisturbed for the immediate postoperative period.

For example, a 2-year-old child with retinal blastoma was put to sleep according to the method I have described and received nitrous oxide and oxygen while the eye was exposed and the radium seeds were implanted. In this case the rectal administration of thiopental sodium (100 mg. per cubic centimeter) was followed in exactly five minutes by injection of the four drugs concerned. Respiration was depressed for one and one-half minutes, no doubt as a result of the peak effect of the five drugs used. In this instance results probably would have been better had I waited a few more minutes before proceeding with the hypodermic injection. Three and one-half hours later the operation was concluded by exposure of the eye and removal of the radium. Under such conditions it probably would be wise to do venipuncture and to administer fluids intravenously throughout the procedure.

By means of this technique a difficult anesthetization problem is handled with ease. A minimum of depression referable to any one single agent will be noted, with a consequent minimal risk to the patient. This again emphasizes the value of the concept of balanced anesthesia.

Comment

I have been assured by pediatricians who refer such patients for the test and by physiologists who do the test that they are entirely satisfied with the results of this method of management, since it helps them to avoid technical errors which might otherwise make it difficult to interpret their data. The excellent respiratory action which the method provides is the result of the effect of levallorphan tartrate.

200 First St. S. W.

Dr. Richard M. Hewitt aided in the preparation of the table.

References

1. Lundy, J. S.: Amnesia-Analgesia for Management of Children Too Young to Cooperate: Method for Use During Cardiac Catheterization and Other Procedures, J. A. M. A. **166**:453-455 (Feb. 1) 1958.

2. Lundy, J. S.: New Methods for Conquest of Pain Through Use of Antagonists and New Management of Analgesia-Amnesia for Cardiac Catheterization in Children Too Young to Cooperate, J. Am. A. Nurse Anesthetists **25**:221-224 (Nov.) 1957. Reference 1.

CLINICAL NOTES

SAFETY CLOSURE CAPS

SAFETY MEASURE FOR PREVENTION OF ACCIDENTAL DRUG POISONING IN CHILDREN

Jay M. Arena, M.D., Durham, N. C.

The accidental ingestion of drugs causes 35% of deaths from poisoning in children 1 to 5 years of age. In this age group the incidence of poisoning from drugs is, however, far greater than that from household agents. Mellins and co-workers [1] reported the incidence of drug poisoning alone from the Chicago Poison Control Center as 50.6%. Recent figures from the National Clearing House, as reported by Cann and associates,[2] showed that 50% of the 4,000 cases reported from 29 poison control centers were due to the ingestion of drugs. Figures from the New York Poison Control Center are even higher—an amazing 70%.[3]

In 1956 over 3.5 billion dollars was spent for drugs in the United States, so there is little wonder that poisoning is so frequent in infants and children who learn by exploration, questioning, sampling, and trial and error. They are particularly susceptible to the accidental ingestion of brightly colored, attractively shaped and packaged, sugar-coated drugs of all kinds. This being the case, it should be apparent to everyone that all available safety measures and precautions should be utilized. It is imperative that physicians give more than lip service to this problem and that they stop suggesting that education is the only means of prevention. Precautionary labeling and safety closures are good measures, among others, in the prevention of these tragic accidents.

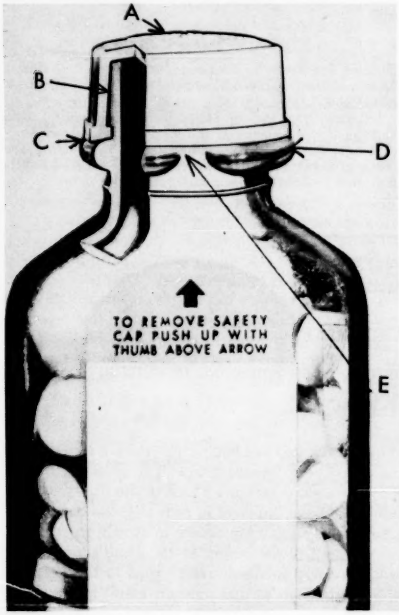
After trying out more than 14 different types of safety caps over a period of three years, two were finally selected for comparison with the conventional screw cap in 1,600 representative homes with children under 5 years of age. The objective of this survey was to determine which of the three closures would be most effective in reducing the chances of small children gaining access to aspirin in the containers kept in the home. At the same time, it also was necessary for these safety caps to be designed and constructed so that mothers could remove and replace them with a reasonable amount of ease and convenience.

Results of Survey

The following information was obtained at the completion of the survey: The A and B closures were equally difficult to remove by over 93% of the children in the survey, as compared to 66% in removing the screw cap. Only 33.8% of the children had difficulty in replacing the B closure, as compared to 56.8% for the A type and 38.9% for the screw cap. These figures imply that older inquisitive children, in replacing the B cap easily, can conceivably prevent younger infants in the family from gaining access to the contents of the respective bottle.

In the survey of mothers, difficulty in removing the closure was affirmed by over 67% for the A type, 16% for the B type, and 49% for the screw cap. When asked, "In regularly replacing the cap, do you feel that it goes on securely each time?" affirmative answers were given by 60% for the A type, 97% for the B type, and 81% for the screw cap.

As a safety measure, the difficulty that mothers encountered in replacing the A cap and the screw cap (i. e., resealing the bottle) is more significant than their difficulty in opening them, since a loose cap can mean an open container.



Safety closure of choice: *A*, wording on top, "Keep bottle out of children's reach," for adult caution; *B*, glass tapers to allow easy cap replacement; *C*, grip of cap under glass for tight seal and reseal; *D*, wide-design special glass bead, to help reduce biting off or pulling off by children; and *E*, bead opening (in front and back) for adult "thumb-off" removal.

The children's difficulty in removing the B cap and their mothers' ease in removing and replacing the B cap made it the closure of choice from the manufacturers' and the families' standpoint (see figure).

Although questionnaire responses are often disapproved of for definitive statistical data, and however impressive these figures are, one must always keep in mind that over 6% of the children under 5 years of age in the survey were able to remove, in one way or another, the B safety cap without great difficulty—many by using their teeth. At any rate, it must be realized that, regardless of what safety measures and precautions are taken, some children will circumvent them in any case.

Summary and Conclusions

A survey of 1,600 families has indicated that a safety closure of plastic is not only practical for manufacturers and mothers but also, if used on all packaged and prescribed medicaments, is a child-safety measure of real importance. The widespread adoption of a safety closure of some type for all drug containers in common home use could reduce in great part the morbidity and mortality from the accidental, experimental, and innocent ingestion of potentially poisonous drugs. Hospitals should lead the way in dispensing drugs only in bottles with a safety closure.

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This study was supported by a grant from Plough, Incorporated, Memphis, Tenn.

References

1. Mellins, R. B.; Christian, J. R.; and Bundeson, H. N.: Natural History of Poisoning in Childhood, Pediatrics **17:**314-325 (March) 1956.

2. Cann, H. M.; Neyman, D. S.; and Nerhulst, H. L.: Control of Accidental Poisoning—Progress Report, J. A. M. A. **168:**717-724 (Oct. 11) 1958.

3. Jacobziner, H., and Raybin, H.: Briefs on Accidental Chemical Poisonings in New York City, New York J. Med. **58:**2097-2100 (June 15) 1958.

FORMALDEHYDE AS A FUMIGANT.—Disinfection by formaldehyde fumigation, unless it is to be inconveniently prolonged, has not the same margin of safety as disinfection by heat or chemical agents in solution. Formaldehyde should not, therefore, be used when any more certain method can conveniently be applied. We should not recommend it for any application where the killing of all pathogenic organisms is imperative, e.g. for surgical instruments, or the disinfection of the bedding of smallpox patients. The three applications for which formaldehyde seems most suitable are the disinfection of: (1) Rooms from which fabrics have been removed. A gas or vapor is commonly the only possible agent for this purpose. (2) Small objects which cannot be heated or wetted without damage, such as respirators, leather goods, boots, and toys not made of fabric. (3) Mattresses and woolen blankets. If these are spread out to allow access of the gas, surface disinfection is possible at room temperature, but if disinfection of the interior of the mattress or of folded blankets is required, some form of heated chamber must be used. —The Practical Aspects of Formaldehyde Fumigation, *Monthly Bulletin of the Ministry of Health,* December, 1958.

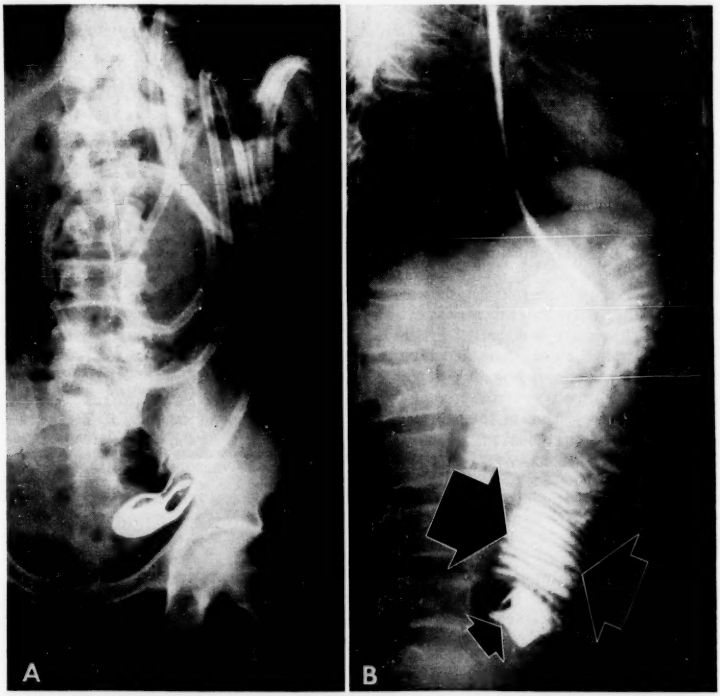
ILEAL INTUSSUSCEPTION AS RESULT OF INTESTINAL INTUBATION

Maxwell H. Poppel, M.D.
and
Bertram Brinsley, M.D., New York

The long intestinal tube commonly employed in a wide variety of conditions has been in use for about 20 years. The single lumen tube was introduced in 1944, at which time mercury began to replace air in the tube's bag.[1] The complications of intubation have been discussed by many authors. The particular one reported in this paper is rare. Smith,[2] reporting on 1,000 intubations, failed to observe a single case of intussusception. Nichols,[1] using the Harris tube, had one case. Dunn and Shearburn [3] quote three cases from the literature and add one case of their own. Wangensteen [4] and Cantor and Reynolds [5] mention the long intestinal tube as a rare cause of intussusception.

From the Department of Radiology of the New York University–Bellevue Medical Center.

Recently such a complication occurred in one of our patients. We are reporting this case because it clearly visualizes the cause and effect and, to our knowledge, possesses the best illustrations of its kind.



A, mercury bag at site of obstruction before administration of diatrizoate. *B*, left lateral view with diatrizoate showing mercury-filled bag as part of intussusceptum (*small arrow*) and widened loop of ileum distal, but located above, acting as intussuscipiens (*large arrows*).

Report of a Case

A 50-year-old man was first admitted in September, 1958, with a presenting complaint of abdominal pain of three days' duration. His history included a duodenal ulcer of 10 years' duration and partial gastrectomy 4 years prior to admission. Since then he had had intermittent abdominal pain. Three days prior to admission he experienced continuous left lower quadrant pain with vomiting of bile-stained fluid. He had fever and leukocytosis. A diagnosis of small intestinal obstruction was made and laparotomy performed the same day. Findings at operation were negative, even though special attention was directed to the entire small intestine.

The postoperative course was uneventful until the ninth day, when the patient complained of abdominal cramps. Abdominal roentgenography revealed small intestinal distention with fluid-filled loops. Decompression of the intestine with a Cantor tube was attempted for four days. Diatrizoate (Hypaque) sodium study through the tube then revealed a complete obstruction in the ileum, with the mercury bag impacted at this site (see figure).

The roentgenologic findings indicated intussusception. The loop containing the mercury bag acted as part of the intussusceptum, while the small intestine loop just beyond was widened and acted as the intussuscipiens.

Immediately after the diatrizoate study he was reoperated on and an ileo-ileo-ileal intussusception was found and reduced, and the involved segment was resected. No significant gross abnormality was noted. The postoperative course was uneventful. The patient was discharged on the 13th postoperative day. Biopsy of the removed ileal segment revealed submucosal edema.

Wangensteen [4] reports intussusception as accounting for 0.4% of all cases of intestinal obstruction. The rarity of intussusception, especially in adults, may be appreciated from the statistics quoted by de Cesare [6]: of 113,351 hospital admissions in Duluth, Minn., there were 22 cases of intussusception but only 1 was in an adult; in 529,897 admissions to the Massachusetts General Hospital, from 1887 to 1946, there were 146 cases of intussusception, of which 43 were in adults.

Deterling and others [7] reported 40 cases of intussusception in adults. In five cases there was evidence that the intussusception was caused by the presence or withdrawal of a long intestinal tube. The clinical and x-ray features that they found most reliable were (1) obstruction to the free flow of barium, (2) marked narrowing of the valvulae at the site of obstruction, (3) gradual narrowing of the lumen proximal to the lesion, (4) local widening of the intestine with semicircular mucosal markings (concentric ring or spiral sheath), (5) palpable mass at the site of obstruction, and (6) changes in position and shape after defecation. In our case findings the first three features were present.

The vast majority of intussusceptions occur in infants, but a small number (5%) occur in adults. In contradistinction to most cases in children, an immediate cause for the intussusception is usually found in the adults, such as tumors or other pathological states of the intestine or its attachments. Among the rarest is an intussusception caused by foreign body or intestinal decompression tube. A search of the American literature reveals only 11 previous case reports involving a tube. The exact mechanism by which a tube causes intussusception is not clearly understood. Harris [8] believed that the distended balloon acted like a polyp, which was also the opinion of Dunn and Shearburn [3] and Cantor and Reynolds.[5]

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References

1. Nichols, H. M.: Intussusception Occurring After Intubation of Small Intestine: Report of Case, Northwest Med. **45**:924-925 (Dec.) 1946.

2. Smith, B. C.: Experiences with Miller-Abbott Tube: Statistical Study of 1,000 Cases, Ann. Surg. **122**:253-259 (Aug.) 1945.

3. Dunn, D. D., and Shearburn, E. W.: Jejunal Intussusception: Unusual Complication of Use of Miller-Abbott Tube, Surgery **26**:833-836 (Nov.) 1949.

4. Wangensteen, O. H.: Intestinal Obstruction: Physiological, Pathological and Clinical Considerations with Emphasis on Therapy, Including Description of Operative Procedures, ed. 3, Springfield, Ill., Charles C Thomas, Publisher, 1955.

5. Cantor, M. O., and Reynolds, R. O.: Gastro-Intestinal Obstruction, Baltimore, Williams & Wilkins Company, 1957.

6. De Cesare, N. F.: Enteric Intussusception in Adult, Am. J. Surg. **77**:532-536 (April) 1949.

7. Deterling, R. A.; O'Malloy, R. D.; and Knox, W.: Intussusception in Adult, with Emphasis on Retrograde Type, A. M. A. Arch. Surg. **67**:854-864 (Dec.) 1953.

8. Harris, F. I.: Intestinal Intubation in Bowel Obstruction: Technique with New Single Lumen Mercury Weighted Tube, Surg. Gynec. & Obst. **81**:671-678 (Dec.) 1945.

HYPERCORTISONISM IN PATIENTS WITH RHEUMATOID ARTHRITIS.—The clinical features of Cushing's syndrome which may be produced in patients receiving adrenal steroids are now familiar to most physicians. These features include fluid retention, moon face, abdominal striae, enlarged supraclavicular and cervicodorsal fat pads, hypertension, diabetes, osteoporosis, purpura, insomnia, hirsutism, excessive appetite, nervous tension, and other symptoms. It has been reported that from 66 to 75 per cent of all patients treated with adrenal steroids will develop one or more of these features. In addition to these usual features, however, many patients with rheumatoid arthritis under long term adrenal steroid therapy have been seen to develop certain unusual or "special" features of hypercortisonism. These special features comprise a syndrome which is characterized by musculoskeletal aching, fatigability, and cyclic mood changes. . . . Furthermore, these patients seem susceptible to so-called "mesenchymal reactions" which may simulate lupus erythematosus, a flare of rheumatoid arthritis, or periarteritis nodosa. Treatment of these special features of hypercortisonism consists in the steady, gradual reduction of dosage in small decrements according to the patient's reaction to the withdrawal.—J. W. Kemper, M.D., Hypercortisonism in Patients with Rheumatoid Arthritis, *Texas State Journal of Medicine*, December, 1958.

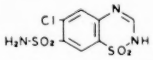
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Chlorothiazide (Diuril).—6-Chloro-7-sulfamyl-1,-2,4-benzothiadiazine-1,1-dioxide. — The structural formula of chlorothiazide may be represented as follows:



Actions and Uses.—Chlorothiazide, introduced commercially in 1958, is a potent, orally effective, nonmercurial diuretic agent. The drug is a potent inhibitor of the renal tubular reabsorption of sodium. In appropriate doses, it causes only a slight increase in excretion of bicarbonate and a considerable increase in the excretion of chloride. Potassium excretion is also increased but to a lesser extent than that of sodium or chloride. Under ordinary conditions of use, chlorothiazide does not alter urinary pH, nor does it cause significant changes in systemic acid-base balance. Its diuretic potency is greater than that of any other orally given nonmercurial diuretic presently available; it is only slightly less effective than parenterally administered mercurials. The mode of action of chlorothiazide in influencing the excretion of sodium and chloride has not been fully defined. Bicarbonate excretion is possible in the lower dose range because of a mild carbonic anhydrase inhibitory effect, but this effect is not responsible for the major excretion of sodium and chloride.

Chlorothiazide is rapidly and uniformly absorbed from the gastrointestinal tract. Its onset of action is rapid; diuretic effects are apparent within 2 hours after oral administration and persist for about 6 to 12 hours. Refractoriness to the drug is relatively uncommon even after prolonged periods of continuous administration.

Chlorothiazide is valuable as an adjunct in the management of congestive heart failure. The drug may be used for the initiation of diuresis as well as for the maintenance of the edema-free state in all types and degrees of severity of cardiac decompensation in which diuresis is required. As with any diuretic, patients with the most severe forms of the disease may be unresponsive to its action, particularly when the glomerular filtration rate is markedly reduced. Chlorothiazide is a satisfactory replacement for other orally given diuretics and can often be used in place of the parenterally administered organic mercurials. Its continued effectiveness makes it useful in many patients either who fail to respond or who have become refractory to other diuretics. Whereas therapy with chlorothiazide is not intended as a replacement for low-salt diets, administration of the drug makes it desirable to liberalize the salt intake in certain patients with congestive heart failure.

Chlorothiazide has been used with good results in the management of edema associated with nephrosis and certain types of nephritis. The drug may be of particular benefit to patients with nephrotic edema to whom corticotropin, glucocorticoids, and other agents which cause sodium retention are being administered concomitantly. If diuretic therapy is indicated in patients with edema caused by renal disease, chlorothiazide has an advantage over acetazolamide or ethoxzolamide in that it is most unlikely to precipitate a metabolic acidosis.

Chlorothiazide has been of value for the management of edema associated with liver disease, particularly portal cirrhosis. The drug has also been used for the treatment of toxemia and edema of pregnancy, for obesity or for premenstrual discomfort associated with fluid retention, and for the edema induced by such agents as corticotropin, adrenal cortical steroids, and certain estrogens.

In addition to its employment as a diuretic, chlorothiazide also is useful as an adjunct in the management of hypertension. When given alone, the drug generally has negligible or minimal lowering effects on the blood pressure. However, it is apparently capable of enhancing the effects of other antihypertensive agents such as Rauwolfia and Veratrum alkaloids, hydralazine, and the ganglionic blocking agents. It may also enhance the hypotensive effects of surgical sympathectomy. The mechanism of action of chlorothiazide in reducing high blood pressure has not been determined. The judicious use of chlorothiazide may make possible a sustained antihypertensive effect while allowing somewhat less rigid restrictions on dietary salt intake. When chlorothiazide is given in combination with other antihypertensive drugs, the dosage

of the latter agents (particularly the ganglionic blocking agents and hydralazine) must be reduced markedly; this decreases or even eliminates certain of the more troublesome side-effects, including those resulting from parasympathetic ganglionic blockade.

Chlorothiazide is apparently well tolerated, and few serious immediate side-effects have been reported to date. It should be borne in mind, however, that the drug is an extremely potent compound in its influence on fluid and electrolyte excretion. It should not be given unless the patient can be regularly and carefully observed for the early signs of fluid and electrolyte imbalance and unless appropriate measures can be taken to prevent such imbalance or to correct it if it occurs.

In some patients, chlorothiazide may produce a hypochloremic alkalosis as the result of excessive excretion of chloride in relation to sodium and a concomitant rise in plasma bicarbonate levels. In these cases, the excretion of potassium is also likely to be excessive so that a hypokalemia is superimposed on the hypochloremic alkalosis. These electrolyte imbalances are more likely to occur during excessive or continued administration of the drug to patients who either fail to show a natriuretic response or, having shown an initial response, do not continue this response. Hypokalemia may result in increased sensitivity to the action of digitalis. Caution must therefore be employed to prevent hypokalemia when digitalis is administered. Changes in the dosage requirements for both digitalis and chlorothiazide must be anticipated. Patients with myocardial ischemia as a result of coronary artery disease may also have a predisposition to serious cardiac arrhythmias if hypokalemia occurs. Hypochloremic alkalosis may be treated by making up the chloride deficiency (ammonium chloride should not be given to patients with hepatic disease). Hypokalemia should be corrected by giving potassium chloride. Both electrolyte disturbances can usually be reversed by the temporary discontinuance of chlorothiazide.

Occasionally the so-called low-salt syndrome may complicate therapy with chlorothiazide in patients with severe congestive heart failure who are markedly edematous. This complication is most likely to occur when excessive amounts of the drug are administered at the same time that dietary salt intake is rigidly restricted. In some cases, it may be necessary to treat this condition with the cautious infusion of hypertonic sodium chloride solutions along with rigid restriction in water intake, even in the presence of intense thirst.

In patients with severe renal or hepatic impairment, as indicated by clinical and laboratory observations, diuretic therapy may be ineffective and even contraindicated.

In patients with advanced cirrhosis, chlorothiazide should be administered cautiously; it may be necessary in some instances to discontinue administration. It should be borne in mind that in certain patients with hepatic disease, particularly those who have a history of a previous episode of hepatic coma or precoma, electrolyte imbalance (among other factors) may precipitate hepatic coma. When chlorothiazide is used in patients with cirrhosis, it may be desirable to place them on a low-protein diet and to administer potassium glutamate by mouth, as well as a broad-spectrum, nonabsorbable antibiotic such as neomycin, to minimize the possibility of coma.

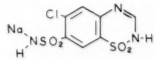
Rare side-reactions to chlorothiazide include nausea, epigastric discomfort, dizziness, weakness, and paresthesias. In occasional instances, a drug rash has been observed. The possibility of allergic reactions arising from sensitivity to the drug should be borne in mind.

Dosage.—Chlorothiazide is administered orally. Dosage must be highly individualized according to the response of the individual patient and the severity of the condition being treated. For diuretic effects, the usual dose for adults ranges from 500 mg. to 1 Gm. once or twice a day. A total daily dose of 1 Gm. or more is usually given in two divided doses. For antihypertensive effects in conjunction with the use of other antihypertensive drugs, the dosage of chlorothiazide ranges from as little as 250 mg. twice daily to 500 mg. three times a day.

Preparations: tablets 250 mg. and 500 mg.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorothiazide.

Chlorothiazide Sodium (Lyovac Diuril).—The sodium salt of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide.—The structural formula of chlorothiazide sodium may be represented as follows:



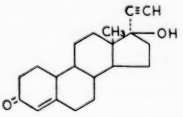
Actions and Uses.—The sodium salt of chlorothiazide, introduced commercially in 1958, has the same actions and uses as the parent substance except that it is more soluble and therefore suitable for parenteral injection. (See the monograph on chlorothiazide.)

Dosage.—Chlorothiazide sodium is administered intravenously. The lyophilized powder is reconstituted with a suitable volume of sterile diluent immediately prior to administration. The drug may be given as a concentrated solution by direct intravenous injection or may be infused slowly by intravenous drip. Dosage is the same as for chlorothiazide.

Preparations: powder (injection) 500 mg.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorothiazide sodium.

Norethindrone (Norlutin). – 17α-Ethinyl-19-nortestosterone.—The structural formula of norethindrone may be represented as follows:



Actions and Uses.—Norethindrone, sometimes referred to as norethisterone, is a highly potent, orally active, progestational agent which was introduced commercially in 1957. It produces the typical physiological and anatomic effects of progesterone and its derivatives, i. e., induction of a secretory endometrium, luteal changes in the vaginal epithelium, disappearance of cervical fern, increases in basal body temperature, and withdrawal bleeding from an estrogen-primed endometrium. When given from the 5th to the 25th day of the menstrual cycle, the drug is believed to inhibit ovulation. Continuous administration of norethindrone can also delay menstruation for prolonged periods, with only occasional instances of breakthrough bleeding. The pseudopregnancy thus induced is presumably an anovulatory amenorrhea. In terms of weight of drug required for progestational effects, norethindrone is one of the most potent agents known. Its onset and duration of action are about the same as with parenterally administered progesterone; if given for five days to amenorrheic women after estrogenic stimulation, the drug will generally induce withdrawal bleeding within 24 to 72 hours after its discontinuance. Animal experiments indicate that norethindrone has slight estrogenic effects; there is no evidence of androgenic activity. However, studies in animals are not adequate to estimate the extent to which observed histological changes may be due to the estrogenic activity of the drug. The drug is apparently not metabolized in the same manner as progesterone, since its administration does not cause an increase in the urinary excretion of 17-ketosteroids.

Norethindrone has been used in the treatment of primary and secondary amenorrhea. The drug will not induce secretory changes in the endometrium, with subsequent menstruation, unless there has been adequate estrogenic stimulation. Hence, in patients with inadequate endogenous estrogen production, as determined by vaginal cytology, estrogen priming is necessary. In women with menstrual irregularity or secondary amenorrhea due to inadequate corpus luteum activity, the monthly employment of norethindrone may help in reestablishing a normal cyclic pattern. This effect may be helpful in the management of patients with infertility problems, since it permits a more accurate prediction of the time of ovulation. Although the ultimate value of progestogens in the treatment of female infertility remains to be determined, agents such as norethindrone might theoretically be of value in establishing conditions conducive to pregnancy by reason of their inhibiting effect on the arborization of cervical mucus (which may act as a barrier to sperm penetration) and by preparing the endometrium for implantation of the ovum. Like other progestogens, norethindrone may be tried in the treatment of functional uterine bleeding, provided that genital malignancy has been ruled out and that curettage has established the diagnosis of benign endometrial hyperplasia.

Because it can induce a state of amenorrhea for as long as its daily administration is continued, norethindrone has been suggested as a means of temporary delay of the menstrual period for honeymoon, vacation, and athletic events. However, the use of a potent hormone to inhibit a normal physiological function, simply for patient convenience, should be discouraged. The menstrual-inhibiting property of the drug may, however, serve a useful purpose in alleviating the symptoms of endometriosis and causing a regression of endometrial implants.

Norethindrone, as well as other progestogens, has been tried in a more or less empirical manner for the treatment of threatened or habitual abortion. At present, there is a dearth of convincing evidence that any agent of this type can reduce the incidence of fetal loss. There is likewise insufficient evidence at hand to establish the proposed use of norethindrone for the treatment of premenstrual tension or dysmenorrhea.

The clinical use of norethindrone has not been associated with any appreciable toxicity. In occasional instances, mild nausea, lethargy, and spotting before the calculated onset or after termination of menstruation have been reported. In young animals, prolonged administration of large doses of the drug causes a decrease in food consumption, with a consequent depression in weight gain; however, anorexia and weight loss have not been a problem clinically. Prolonged therapy with norethindrone generally decreases libido, an effect that would negate its proposed use to delay menstruation during the honeymoon.

Dosage.—Norethindrone is administered orally. For amenorrhea, menstrual irregularity, functional uterine bleeding, and infertility, the usual dose is 10 to 20 mg. daily from the 5th to the 23rd day of the menstrual cycle. A five-day period is allowed for withdrawal bleeding to occur. Continuous daily doses of 20 to 30 mg. are usually sufficient to prevent menstruation. For the treatment of premenstrual tension and dysmenorrhea, the proposed dose is 10 mg. once or twice daily, beginning in the preovulatory phase and continuing to the 20th to the 23rd day of the cycle. Pending more evidence to show a beneficial effect, the proposed dosage for these latter purposes is considered experimental.

Preparations: tablets 5 mg.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of norethindrone.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

ABUSE OF ANTIBIOTIC LOZENGES

ELSEWHERE IN this issue of THE JOURNAL (page 1235) a correspondent directs attention to the development of moniliasis of the soft palate and pharynx, sometimes fatal, after the use of antibiotic lozenges. Although antibiotic lozenges enjoy a degree of popularity in the local treatment of diseases of the throat, it is known that effective concentration of the contained medication cannot be maintained for long periods on the surface of the tonsils or pharynx because of the continual washing effect of saliva. There is no such response as rendering the throat sterile, or even antiseptic, except possibly for a short time.

In superficial infections of the throat, local administration of antibiotic and chemotherapeutic agents may be effective. However, their value diminishes if the micro-organisms have penetrated into the tissues. Actually, once micro-organisms have established themselves below the surface, and an abscess has formed, locally applied medicaments have little value. In acute streptococcic tonsillitis, for example, all of the offending organisms are not found on the surface of the tonsils—in reality, many of them lie deep in the tonsillar tissues. Under such circumstances, the value of lozenges, troches, pastilles, and medicated chewing gum is dubious. Deeply seated bacteria are best approached systemically. It is dangerous to rely on local medication alone in the treatment of severe infections of the throat.[1]

Inadequate dosage and indiscriminate usage of topical antibiotic and sulfonamide compounds in the treatment of infectious diseases of the throat can breed resistant bacterial strains. Their promiscuous use is unwarranted in trivial infections; moreover, their use is limited from time to time by the development of allergic reactions, by the sensitiveness of patients to these agents, by the acquisition of antibiotic-resistance and sulfonamide-resistance states, and by their ability to mask symptoms occasionally. Finally, stomatitis has been traced to various antibiotics and sulfonamides present in a variety of lozenges, troches, pastilles, and medicated chewing gum.

THE PHYSICIAN'S ROLE IN SAFE DRIVING

In this issue of THE JOURNAL, page 1195, is a report prepared by the Committee on Medical Aspects of Automobile Injuries and Deaths which will be of value to physicians called on to advise whether or not an individual is capable of driving a motor vehicle safely.

It can easily be determined if the individual meets the physical standards for driver licensing established by the state licensing authority. These standards lend themselves to precise measurement. Not easily measured and not well understood in the production of automobile accidents are factors such as poor judgment, emotional disturbances, and faulty attitudes.

Injuries suffered in automobile accidents are an important health problem in the United States. About 37,000 persons were killed in automobile accidents in 1958 and about 5 million were injured seriously enough to require medical attendance or restriction of their activity for one day or longer.

Most automobile accidents occur because of human failures. Many drivers are physically, mentally, emotionally, or physiologically impaired, sometimes only temporarily, sometimes permanently. The evaluation of impairment in relation to safe driving ability is best done by physicians. It is the purpose of the guide, which this committee prepared after some two years of study, to assist the physician in his evaluation.

The number of registered vehicles, the number of licensed drivers, and the number of miles driven are steadily increasing. Exposure to motor vehicles occurs daily in the lives of the majority of Americans. The many groups working in the accident prevention field are trying to see that this exposure does not result in injury. Physicians can make a great contribution in automobile accident prevention by determining the fitness of drivers to operate motor vehicles.

1. Fabricant, N. D.: Modern Medication of Ear, Nose and Throat, New York, Grune & Stratton, Inc., 1951.

ORGANIZATION SECTION

MEDICAL GUIDE FOR PHYSICIANS IN DETERMINING FITNESS TO DRIVE A MOTOR VEHICLE

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Prepared by the Committee on Medical Aspects of Automobile Injuries and Deaths, American Medical Association. Committee members are Fletcher D. Woodward, M.D., Chairman, Charlottesville, Va.; Horace E. Campbell, M.D., Vice-chairman, Denver, Colo.; Jacob Kulowski, M.D., St. Joseph, Mo.; Harold M. Brandaleone, M.D., New York; John R. Rodger, M.D., Bellaire, Mich.; Seward E. Miller, M.D., Ann Arbor, Mich.; Ross A. McFarland, Ph.D., Boston; James L. Goddard, M.D., Washington, D. C.; and Howard N. Schulz, Secretary, Chicago.

Introduction

Traffic accidents killed about 37,000 individuals in 1958 and injured about 1,350,000, according to the National Safety Council. These data were developed from the reports of official agencies. The data refer to the number of injuries causing disability beyond the day of the accident. The U. S. Public Health Service has estimated that there are about 4,700,000 injuries annually in automobile accidents. This estimate was based on the National Health Survey of 1957-1958 which derived its data from household interviews. Persons with injuries involving one or more days of restricted activity or medical attendance were included. On the basis of the latter figure it has been predicted that 1 person in every 10 in this country will be injured or killed in a motor vehicle accident within the next four years. This constitutes one of the nation's largest unsolved health hazards.

It is the purpose of this guide to call attention to the areas in which the medical profession may be of help in combating this serious health problem. This guide has been prepared to assist physicians in examining patients and advising them on their ability to operate a motor vehicle safely. Physical, mental, and emotional states or disabilities likely to impair driving ability are specifically enumerated along with the problems of temporary incapacities from medicaments and alcohol.

The physical and mental demands of the task of driving vary greatly with the type of vehicle and the type of driving. For this report, three types of vehicles have been considered—the private motor vehicle, the commercial vehicle, and the passenger transport vehicle. The driver of the commercial or passenger transport vehicle cannot usually choose the hours he will drive nor the route he will take. The driver of the private vehicle may, in many cases, select both the time of his travel and the route. The driver of the commercial or passenger transport vehicle will spend more hours daily in driving than most drivers of private vehicles. There is little similarity between the demands on the resources of the individual who drives half a mile to the store on a rural road with no intersections and the individual who drives in rush hour traffic in a metropolitan area. The physician should keep these matters in mind when advising his patients on their fitness to drive.

All states but one have laws concerning the physical requirements for driver licensing. Every physician should be familiar with the laws, and his advice to patients must be consistent with the laws of the state in which his patient is licensed.

Human failure overshadows all other factors in the production of highway accidents. The human mechanism must be in good condition to cope with the split second timing needed to maneuver responsive high speed motor vehicles. There is no doubt that poor judgment, impaired reaction time, faulty attitudes, emotional disturbances, and physical disabilities, including impairment of the sensory organs, are basically responsible for most accidents. Thus, the key to ultimate success in automobile accident prevention lies in the driver—his intelligence, his sense of personal and social responsibility, his reactions to various stimuli in normal conditions and under stress, and his driving ability in good health and in illness.

The physician is qualified by training to ascertain the physical, mental, emotional, or physiological impairments of an individual. Moreover, he is in a good position to evaluate these impairments in relation to safe driving ability. Obviously, it is not always easy to arrive at a decision in these cases. Variations in severity of illness or impairment, variations in individual reactions and adjustment, and variations in individual response to medicaments are significant factors in evaluating each case. However, even in the realm of behavior patterns, the physician is in an ideal position to do effective counseling by translating scientific data into terms of lay understanding. Few patients realize the small amounts of alcohol required to impair dangerously their driving ability or that alcohol is involved in about 50% of automobile accidents with fatalities; nor does the slightly inebriated driver realize that he materially increases his likelihood of a serious accident.

A conscientious individual may inquire, "Doctor, is it all right for me to drive an automobile in my condition?" This situation usually is conducive to a receptive patient attitude if perchance the advice may be "bad news." Frequently, it may be necessary for an equally conscientious physician, recognizing his responsibility for the safety of his patient and the public, to caution the patient against driving for a certain period of time or even permanently, unhappy as this may make the patient. Many of these conditions have been graphically described for the lay public in a previous publication of this Committee, entitled "Are You Fit to Drive?" Physicians should find this descriptive pamphlet (available from the Association of Casualty and Surety Companies, 60 John St., New York 38) helpful in dealing with adamant patients.

When physicians discover any conditions in their patients which might make it inadvisable for them to drive a motor vehicle, they should advise the patients to report the condition on the next application for renewal of the driver's license. This is for the patient's own protection. If this information is not reported on the application and the applicant subsequently becomes involved in an accident to which the condition either directly or indirectly might be a contributing cause, in many states the insurance company may legally refuse liability.

This guide is devoted to the physician's role in helping prevent motor vehicle accidents through appropriate advice and treatment to patients. However, it is recognized that many accidents will continue to occur. Therefore, the Committee also is interested in preventing, as much as possible, personal injury to the occupants of vehicles involved in accidents.

The elimination of many road hazards by improved highway design and construction is proceeding at a fast pace. Also, there has been great improvement in the maneuverability, responsiveness, and speed of acceleration and deceleration of automobiles. In the construction of the motor vehicle lies a great opportunity for the prevention of serious injury to the occupants when accidents do occur. It is possible to design, build, and equip an automobile so that injury or death will occur only in the more extreme crashes. In a car so designed and equipped, personal injuries and deaths would be minimized although accidents continue to occur. It is obviously simpler mechanically to change the design of automobiles to protect frail man than it is biologically to change the design of man to resist traumas—therefore the present urgency for automotive engineers to lend their great talents to this end. Of course, the public needs to understand, accept, and be willing to pay for such design and mechanical changes.

It is probable that the next decade will see a greatly increased emphasis upon more stringent physical standards for driver licensing. It is believed that more and more patients will turn to their physicians for advice and assistance in this regard. In a subsequent publication, this Committee will recommend physical standards for driver licensing and for the guidance of licensing authorities and physicians.

Medicine

Fever, fatigue, metabolic diseases, effects from various drugs, and carbon monoxide poisoning are among the medical conditions adversely affecting driving ability. Cardiovascular disease and alcohol are dealt with in separate sections. Physicians should be familiar with the entities here described.

Assessing Safe Driving Ability.—In general, the individual should be assessed medically to determine the answers to the following questions: 1. Has the patient the physical and mental ability to manipulate the controls? 2. Is the patient likely to suffer excessive fatigue that will impair his driving

ability? 3. Does the patient have the required vision and hearing for safe driving? 4. Has the patient any physical or mental disorder likely to cause confusion or a sudden loss of consciousness while driving? 5. Is the patient likely to suffer a temporary impairment of mental, physical, or functional capacity due to alcohol, drugs, infections, or medical treatment, etc., making it unsafe for him to drive? 6. Does the patient have good emotional control or has he signs of antisocial behavior or an emotional disturbance making it unsafe for him to drive?

Metabolic Diseases.—Disturbances in function of the endocrine glands cause many varied symptoms from generalized asthenia, muscle weakness, and spasm or tetany to sudden episodes of vertigo or unconsciousness. Individuals so afflicted should be advised not to drive a motor vehicle until these symptoms have been controlled by appropriate therapy. The more important conditions likely to impair the driving ability of such patients are discussed briefly:

Diabetes Mellitus: Patients suffering from diabetes mellitus of a degree that can be controlled adequately by diet alone may drive any type motor vehicle. Also older individuals with mild diabetes controlled by diet and a sulfonylurea type drug who experience no reactions from the drug may drive any type motor vehicle. If insulin is required and the diabetes well controlled, the individual may drive a private vehicle. However, he should be advised not to drive a commercial or passenger transport vehicle because of the possibility of a sudden attack of hypoglycemia. The uncontrolled diabetic should be advised not to drive any type motor vehicle because of the development of disabling complications. On the other hand, an individual with true renal glycosuria may safely drive any type motor vehicle.

Hyperinsulin States: Individuals suffering from recurring spontaneous attacks of hypoglycemia, pancreatic islet cell adenoma, or other organic or functional causes should be advised not to drive any type of motor vehicle while subject to an attack of faintness, giddiness, or unconsciousness. Patients with mild cases who never develop unconsciousness or disabling symptoms of faintness may drive a private vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Thyroid Disease: In addition to having tachycardia, exophthalmos, and tremor, patients with hyperthyroidism are prone to emotional disturbances, anxiety, and even psychotic symptoms. Therefore, individuals with thyrotoxicosis should be advised not to drive any type of motor vehicle until the disabling symptoms are well controlled. In addition, individuals suffering from an enlarged thyroid gland with pressure symptoms should be advised not to drive a commercial or passenger transport vehicle, although usually they can drive a private vehicle. Individuals with marked myxedema or cretinism should be advised not to drive a motor vehicle.

Hyperparathyroidism and Hypoparathyroidism: Individuals suffering from hyperparathyroidism with muscular weakness and hypotonia should be advised not to drive a motor vehicle. When symptoms are mild or well controlled by therapy, these individuals may drive private motor vehicles but not commercial or passenger transport vehicles.

Individuals suffering from acute hypoparathyroidism with increased neuromuscular excitability, cramps, spasm, and generalized tetany should be advised not to drive a motor vehicle. Chronic hypoparathyroidism varies greatly in its manifestations and severity. Persons with mild cases without tetany may drive private motor vehicles but should be advised not to drive commercial or passenger transport vehicles. However, with the development of tetany, muscular weakness, or ease of fatigue, these patients should be advised not to drive any motor vehicle.

Posterior Pituitary Insufficiency: Individuals suffering from diabetes insipidus should be advised not to drive a commercial or passenger transport vehicle. Under careful medical supervision they may drive private motor vehicles unless visual disturbances or other disabling central nervous system symptoms develop.

Anterior Pituitary Insufficiency: The severe carbohydrate deficiency and spontaneous hypoglycemic episodes that characterize hypopituitary cachexia (Simmond's disease) make it mandatory that these individuals should not drive any motor vehicle. Under close medical supervision, those persons making a good recovery and without hypoglycemic episodes may drive a private motor vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Acromegaly: With the development of muscular weakness and pain, ease of fatigue, cardiac enlargement, and intractable headaches, patients with acromegaly, or gigantism, should be advised not to drive any motor vehicle. Moreover, about 50% of these patients develop visual disturbances which also make it unsafe for them to drive.

Adrenal Cortical Hyperfunction: Patients with adrenal cortical hyperfunction (Cushing's disease), who develop muscular weakness and osteoporosis, should be advised not to drive a motor vehicle. Good recovery after appropriate therapy enables these individuals again to drive a private vehicle. However, they should be advised not to drive a commercial or passenger transport vehicle.

Adrenal Cortical Hypofunction: Patients with well-developed cases of adrenal cortical hypofunction (Addison's disease), particularly those with asthenia and/or persistent low blood pressure, should be advised not to drive a motor vehicle.

Persons with mild cases or those whose symptoms of asthenia and low blood pressure are well controlled by therapy may drive a private vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Hyperfunction of Adrenal Medulla: Hyperfunction of adrenal medulla occurs with the development of pheochromocytoma tumor which clinically is characterized by attacks of headache, dizziness, weakness, and blurring of vision with a rapid pulse and elevated blood pressure. Until completely free of these attacks by removal of the tumor, such individuals should be advised not to drive a motor vehicle.

Drugs.—Numerous drugs, either self-administered or taken at the direction of a physician, produce reactions in some individuals impairing that individual's ability to drive a motor vehicle. The degree of impairment varies tremendously, depending on the severity and type of reaction. Physicians administering drugs likely to produce reactions impairing sensory, mental, or physical functions have a clear responsibility to fully inform their patients concerning this matter, especially as it effects their ability to drive a motor vehicle.

In addition, some patients experience unusual reactions to drugs that ordinarily do not produce disabling symptoms. Physicians must ever be alert to this possibility. Should unusual reactions, allergic or otherwise, occur which impair sensory, mental, or physical functions making it unsafe to drive, the physician must advise the patient not to drive a motor vehicle until the disabling symptoms have been eliminated. The more important groups of drugs likely to impair driving ability are discussed briefly.

Central Nervous System Depressants: The drowsiness induced by analgesic drugs sufficiently impairs driving ability so that patients with such drowsiness should be advised not to drive a motor vehicle. In addition, morphine, its derivatives, and the synthetic narcotics, such as meperidine (Demerol) hydrochloride, cause varying amounts of euphoria, inability to concentrate, apathy, dimness of vision, and rapid flow of uncontrolled thought. Patients under the influence of these drugs should be advised not to drive a motor vehicle.

Hypnotics, Sedatives, and Anesthetics: Hypnotics, sedatives, and anesthetics not only depress central nervous system activity, producing drowsiness and sleep, but also they may produce motor and sensory changes. No doubt small doses of some of these drugs, quieting a highly excited and "jittery" patient, may actually temporarily improve his driving ability. However, this is not the usual circumstance. Therefore, it is best to advise patients taking hypnotic doses of these drugs not to drive a motor vehicle. Patients receiving mild sedation who experience no drowsiness may drive. Of course, a barbiturate addict is incapable of driving a motor vehicle safely. Patients receiving barbiturates and local anesthetics for minor surgery should be advised not to drive.

Tranquilizing Drugs: During the initial period of administration of tranquilizing drugs, such as meprobromate, chlorpromazine, and reserpine, some drowsiness is frequently experienced. Also, with large doses, the accompanying hypotension may occasionally produce short episodes of faintness or giddiness. Therefore, during the initial phase of dosage adjustment, the patient should be advised not to drive a motor vehicle if he is experiencing drowsiness or faintness. At all times these patients should be carefully observed for symptoms of drowsiness or faintness. Patients stabilized on a maintenance dosage of these drugs, who are without symptoms of drowsiness or episodes of faintness, may drive a private motor vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Central Nervous System Stimulants: Although central nervous system stimulants, such as amphetamines, temporarily increase alertness and efficiency, large doses in some individuals may produce headache, dizziness, agitation, irritability, and a decreased ability to concentrate. In all individuals, a period of fatigue and depression follows the initial stimulation. In rare instances an individual may take one of these drugs to prolong the period of alert driving. The dosage should not be more than 5 or 10 mg. and without repetition that day. Drugs of this type should be used only on advice of a physician.

Antihistamines and Drugs Preventing Motion Sickness: There is great individual difference in reaction to antihistamines and drugs preventing motion sickness, with dizziness or drowsiness occurring fairly frequently. Moreover, it is unpredictable in which individuals these symptoms will occur. Patients under medication with these drugs should be advised not to drive a motor vehicle until it has been established by prior trial that they do not experience dizziness or drowsiness.

Anti-infective Agents: In full and prolonged dosage with anti-infective agents, there may occur undesirable reactions of nausea, loss of sense of balance with dizziness, ringing in the ears, and deafness. A patient developing such symptoms should be advised not to drive a motor vehicle. Patients receiving over 1 Gm. of streptomycin daily should be watched carefully for the development of adverse symptoms.

Sulfonamides: Patients receiving sulfonamides should be warned that if they develop any drowsiness or dizziness they at once should cease driving a motor vehicle.

Hallucinogens: Hallucinogens, such as marijuana, have singular abilities for changing normal emotional reactions even causing individuals to become

oblivious or indifferent to their surroundings. Individuals under the influence of these drugs should be advised not to drive a motor vehicle.

Fatigue.—Fatigued, drowsy, and sleepy drivers are responsible for many accidents. They are unable to make split second decisions, reaction time is slowed, and there is loss of peripheral vision and attention. In addition, many individuals are victims of "highway hypnosis," or hallucinations, some after only a few miles of monotonous superhighway driving. Among commercial and passenger transport drivers, most accidents occur within a few hours after the start of a trip. This is due, in part, to their off-duty activities. Thus, all drivers should be cautioned against driving after inadequate rest. Moreover, persons who periodically develop "highway fatigue" should be advised against driving a commercial or passenger transport vehicle.

Because of the development of fatigue, patients should be advised not to drive over eight hours in one day. The vehicle should not be kept too warm, and on continuous drives the operator should be advised to stop, get out, and walk around every two or three hours. In some instances, despite partial fatigue, a driver must proceed. Caffeine in the form of coffee, cola drinks, or tablets will help some individuals. In the rare case where prolonged driving is necessary, a central nervous system stimulant such as benzedrine may be used, but physicians should be very cautious in prescribing stimulants for this use.

Fever and Infectious Diseases.—Patients in the fever stage of an infectious disease should be advised not to drive because of decreased attention and impaired judgment and reaction time.

Carbon Monoxide.—The adverse effect of carbon monoxide, from exhausts and from smoking, on driving ability is in decreasing the visual sensitivity of the eye in areas of low illumination. The relative oxygen deficiency from smoking three cigarettes is equal to that of traveling at a 7,500-ft. altitude. Since adequate ventilation does not take care of chain smokers who inhale, drivers should be advised to refrain from frequent smoking prior to and during periods of night driving or at high altitudes.

Cardiovascular Disease

The examination of the cardiovascular system in determining a patient's ability to drive a private, commercial, or passenger transport vehicle should consist of a complete cardiac history and physical examination. The history should establish presence or absence of edema, orthopnea, cyanosis, dyspnea, and substernal or precordial pain. Also, a history of rheumatic fever, congenital deformities, thyroid disease, syphilis, hypertension, and anemia should be sought.

In order that the cardiovascular system be properly evaluated, the entire body must be examined, including the fundi, lungs, abdomen, and extremities. The physical examination, including palpation, percussion, and auscultation of the heart, should determine if venous congestion, cardiac enlargement, or valvular disease is present. The heart rate, rhythm, and level of blood pressure should also be ascertained.

Urinalysis, blood count, sedimentation rate, and serologic tests for syphilis should be done. Cardiac fluoroscopy, chest x-ray, and an electrocardiogram complete the examination of the cardiovascular system. In evaluating the cardiac status of an individual, it is important to ascertain the presence of cardiovascular disease and then its status according to cause, anatomic defects, physiological abnormalities, and functional capacity.

The lack of conclusive statistical data concerning the role of each cardiac condition as a potential driving hazard is recognized. However, on the basis of knowledge of pathological physiology and the clinical course of these cardiac conditions, it is believed that a medical opinion can be formulated as to the potential driving hazard. These hazards include sudden death, lapse of consciousness, and pain sufficient to cause loss of control of the car.

Etiological and Anatomic Classification.—The principal disabling cardiac conditions and their significance in relation to the safe operation of a motor vehicle are portrayed. It is hoped that this material, presented on (1) an etiological and anatomic basis and (2) a physiological and functional capacity basis, may serve as a basic guide for physicians in their evaluation of such patients.

Rheumatic Fever: Any evidence of active rheumatic fever calls for marked restriction of activity. Therefore, such a patient should be advised not to operate a motor vehicle.

Rheumatic Heart Disease: Appraisal must be made of the extent of damage in connection with valvular deformity, derangements of rhythm, progressive cardiac enlargement, and myocardial insufficiency. Aortic stenosis, when marked, is prone to lead to angina pectoris, syncope, or sudden death. Patients with significant aortic stenosis should be advised not to operate a motor vehicle. Patients with lesser degrees of aortic stenosis without symptoms of angina or syncope should be advised not to operate passenger transport vehicles but may operate a commercial or a private motor vehicle. Patients with aortic insufficiency and left ventricular failure with dyspnea or paroxysmal nocturnal dyspnea should be advised not to operate a motor vehicle. Patients with lesser degrees of aortic insufficiency without dyspnea should be advised not to operate passenger transport vehicles but may operate a commercial or private motor vehicle.

Patients with myocardial insufficiency due to mitral stenosis or insufficiency should be advised not to operate either commercial or passenger transport vehicles but may continue to operate a private vehicle when the myocardial failure is well controlled by therapy with only minimal dyspnea on exertion. Valvular deformity due to rheumatic fever involving the tricuspid and pulmonic valves is less common. Patients with evidence of right-sided heart failure should be advised not to operate either commercial or passenger transport vehicles. If the heart failure is controlled by therapy, the patient may operate a private motor vehicle. A superimposed subacute bacterial endocarditis necessitates immediate treatment and abstinence from operating any motor vehicle.

Disturbances of rhythm are frequent complications of rheumatic heart disease. Uncontrolled auricular tachycardia, flutter, or fibrillation with a rapid ventricular rate is apt to be associated with a diminished cardiac output, severely incapacitating the patients, and therefore they should not operate any motor vehicle. However, when well-controlled by therapy, such patients may operate a motor vehicle. Because of the work load and stress on the heart and the danger of embolization, patients having auricular fibrillation should be advised not to operate commercial or passenger transport vehicles.

Hypertensive Cardiovascular Disease: The upper limit of normal blood pressure is considered to be 150-160/90 mm. Hg. Many patients have labile blood pressures and particularly when seen on the first examination in the office may show levels of pressure above this. If the blood pressure is consistently above 150-160/90 mm. Hg., fixed hypertension must be considered to be present and its cause should be ascertained. Hypertension in itself is not disabling for the safe operation of a motor vehicle, but the complications arising from hypertension, i. e., damage to brain, eyes, heart, or kidneys, may well prove to be so disabling. When the complications of hypertension are limited to the optic fundi, the degree of impairment of driving ability should be evaluated solely on the basis of loss of vision. If there is any evidence that the hypertension has caused cardiac damage resulting in congestive heart failure or angina pectoris, such patients should be advised not to operate a motor vehicle, unless the congestive failure or angina is well controlled by therapy.

Arteriosclerotic Heart Disease: Sclerosis of the coronary vessels results in diminution of blood flow, particularly during exertion, with insufficient nourishment of the myocardium, resulting in angina pectoris. If the original attacks are mild, infrequent, and controlled with therapy, such patients may still drive private motor vehicles but not commercial or passenger transport vehicles.

More prolonged episodes of inadequate myocardial nourishment and substernal pain are termed coronary insufficiency. Arteriosclerotic heart disease may also result in various abnormalities of conduction with varying degrees of heart block, ventricular premature contractions, or arrhythemias. Patients with such symptoms well controlled by therapy may drive private motor vehicles. They should not operate commercial or passenger transport vehicles.

Syphilitic Heart Disease: Patients with syphilitic aortitis having syncope, congestive heart failure, or angina pectoris should be advised not to operate a motor vehicle. If syphilitic aortitis has led to the development of aortic insufficiency, then careful evaluation should be made of the patient concerning the presence of angina pectoris, syncopal attacks, left ventricular enlargement, or congestive heart failure. If any of these have occurred, the patient should not operate commercial or passenger transport vehicles, and, unless the symptoms are well controlled by therapy, the patient should be advised not to operate a private motor vehicle.

Bacterial Endocarditis or Endarteritis: Patients with acute bacterial endocarditis under vigorous treatment are so ill and their activities so restricted that they should not consider operating a motor vehicle. In addition, patients with subacute bacterial endocarditis, because of the danger of embolization to the brain, should be advised not to operate a motor vehicle.

Metabolic Heart Diseases: Patient with thyrotoxic or beriberi heart disease or with severe anemia with impairment of oxygenation of the myocardium or myxedema heart disease, when severely ill, are so incapacitated that they should be advised not to operate a motor vehicle.

Congenital Heart Disease: Some cases of congenital heart disease, such as patent ductus arteriosus, coarctation of the aorta, tetrology of Fallot, and septal defects are amenable to surgical treatment. If signs of myocardial insufficiency are present, such patients should be advised not to operate a commercial or passenger transport vehicle but may operate a private vehicle unless symptoms of myocardial insufficiency are pronounced. Asymptomatic congenital heart lesions are of no significance.

Cor Pulmonale: Patients with right-sided heart failure secondary to disease of the lungs with venous distention, enlargement of the liver, ascites, and edema should be advised not to operate commercial or passenger transport vehicles. However, if the symptoms of right ventricular failure are mild and well controlled by therapy, such patients may operate private motor vehicles.

Myocarditis: Any evidence of active myocarditis due to rheumatic fever, diphtheria, or other causes requires bed rest, and such patients should therefore be advised not to operate motor vehicles.

Arterial Aneurysms and Arteriovenous Fistulas: Any patient having an arterial aneurysm, because of the danger of its rupture, should be advised not to operate any motor vehicle. Arteriovenous fistulas may result in heart failure which, if severe, will be a contraindication to the operation of any motor vehicle. Both conditions may be amenable to surgical treatment.

Diseases of the Pericardium: In the acute phase of pericarditis, patients under therapy are unable to operate any motor vehicle. Benign infectious pericarditis of unknown cause does not constitute a contraindication to the operation of a motor vehicle, once the acute phase has subsided.

Chronic Constrictive Pericarditis: Patients having severe cases with venous distention, enlargement of the liver, and peripheral edema should be advised not to operate a commercial or passenger transport vehicle. If the condition is well controlled by therapy, patients with chronic constrictive pericarditis may operate a private motor vehicle safely.

Cerebral Vascular Disease: Patients with inadequate blood flow to the brain because of arteriosclerosis of the cerebral vessels are apt to have attacks of syncope or dizziness and should be advised not to operate a motor vehicle. If there have been cerebral hemorrhages, thrombosis, infarctions, transient cerebral vascular spasms, or small areas of cerebral softening with resulting changes in personality, alertness, ability to make decisions, or if there has been actual loss of motor or sensory power, or coordination, such patients should be advised not to operate a motor vehicle. If the resulting changes in function are minimal, with little or no disability, it may be possible for these individuals to drive a private motor vehicle.

Diseases of the Veins: Patients with active thrombophlebitis or a previous thrombophlebitis with resulting edema of the extremities and impairment of use should be advised not to operate a commercial or passenger transport vehicle, and, if sufficient disability exists, they should be advised not to drive a private motor vehicle. Patients with active phlebothrombosis should be advised not to drive a motor vehicle because of the danger of embolization with pulmonary infarction.

Physiological Abnormalities.—Physiological abnormalities and disturbances of functional capacity now will be considered in relation to safe driving.

Cardiac Enlargement: Enlargement of either the right or left ventricle should not in itself be considered a contraindication to the operation of a motor vehicle, but such enlargement does point to the presence of organic heart disease which deserves evaluation.

Diminished Cardiac Reserve: Minor degrees of impairment of function of the myocardium will result in dyspnea on exertion. If this is minimal it should not be a contraindication to the operation of a motor vehicle. If myocardial insufficiency is more marked so that dyspnea prevents the performance of the usual duties involved in the operation of a commercial motor vehicle or is likely to prevent proper performance under emergency conditions, then such patients should be advised not to operate commercial or passenger transport vehicles. If the congestive heart failure is well controlled by therapy, these patients may operate a private motor vehicle. These same considerations apply to either hepatomegaly or peripheral edema resulting from myocardial insufficiency.

Arrhythmias and Conduction Disturbances: Auricular premature beats are of little consequence and do not preclude the operation of motor vehicles. Patients with paroxysmal auricular tachycardia, flutter, or fibrillation with myocardial insufficiency should be advised not to operate a commercial or passenger transport vehicle. If such attacks are well controlled by therapy, then the patients may operate any motor vehicle. Auricular fibrillation of a chronic nature provides the risk of embolization from the auricles, and such patients therefore should not operate commercial or passenger transport vehicles.

Ventricular arrhythmias other than occasional ventricular extrasystoles are usually associated with serious heart disease and frequently are the cause of sudden death. Such patients should be advised not to drive commercial or passenger transport vehicles but may drive private vehicles.

Auriculoventricular block, if of minor degree, is of no significance. Patients with prolonged degrees of atrioventricular block or complete atrioventricular block, if associated with convulsive disorders due to Stokes-Adams syndrome, should be advised not to operate a motor vehicle. If these attacks are controlled by therapy, such patients may operate private motor vehicles.

Pain due to Coronary Arterial Insufficiency: Angina pectoris, coronary insufficiency, and myocardial infarction are all indications of impaired blood supply to the myocardium. Such patients should be advised not to operate commercial or passenger transport vehicles. If angina pectoris is mild and controlled by therapy, then such patients may operate their private motor vehicles. The same is true for patients recovering from a myocardial infarction.

Pain due to Pulmonary Hypertension: The significance of pain due to pulmonary hypertension is primarily in differentiating it from pain due to coronary arterial insufficiency. Patients with pulmonary hypertension are not as prone to sudden death and therefore may, if the degree of pain is not too severe or when well controlled by therapy, operate any type of motor vehicle.

Hypertension: The presence of an elevated blood pressure, due to any cause, above 150-160/90 mm. Hg in itself should not be considered as a contraindication to the operation of a motor vehicle. Com-

plications of hypertension do result in disability contraindicating operation of a motor vehicle. Usually persistent hypertension above 180/100 mm. Hg is accompanied by complications that may be dangerous to driving. Such patients must be examined very carefully to make sure that there has been no involvement of the eyes, brain, heart, or kidney likely to prove disabling for the safe operation of commercial or passenger transport vehicles. When such severe impairment or disability exists, the patient should be advised not to operate private motor vehicles.

Hypotension: Hypotension in itself is not a contraindication to the operation of a motor vehicle. If hypotension results in attacks of syncope, such patients should be advised not to operate a motor vehicle. When these attacks are controlled by therapy, patients may operate a private motor vehicle.

Carotid Sinus Sensitivity: Individuals with carotid sensitivity who experience attacks of syncope should not drive a motor vehicle.

Ophthalmology

Adequate vision is essential for the proper and safe operation of a motor vehicle. Visual potentials can be ascertained by using available vision testing instruments.

Licensing authorities have established visual acuity requirements ranging from 20/30 to 20/70. Two states have no specific visual requirements. Every physician should familiarize himself with the visual requirements of his state's licensing authority.

The patient's perception of what he sees is of great importance. As yet, however, there is no practical way of testing for faulty perception. It is important for drivers to have their vision periodically evaluated, particularly those with significant progressive visual deterioration.

Visual Acuity.—At present we believe that patients whose corrected vision, tested under standard conditions, is 20/40 or better may be advised that this vision is adequate for the task of operating a private vehicle. Those with vision less than 20/40 should be referred to an ophthalmologist to ascertain if vision can be improved. Patients with less than 20/70 corrected vision in the better eye should be advised not to drive.

At present there is no uniformity of opinion regarding the safe driving ability of individuals with visual acuity between 20/40 and 20/70. Furthermore, there are no scientific data available which permit the establishment of fixed standards.

The physician, in serving the best interests of these patients, should consider the conditions under which each patient drives and the vision the patient possesses. He is then in a position to advise the patient whether or not he should drive in congested traffic, in hazardous road conditions, at high speed, or at night. It is hoped that continuing research in this field will lead to a more exact basis upon which to advise patients.

The one-eyed or aphakic driver presents special problems. Many individuals in this category acquire judgment of distance and develop the ability to drive safely. Those individuals who have not acquired this judgment should be advised not to drive and to consult an ophthalmologist.

Regulations for licensing drivers of commercial and passenger transport vehicles usually require higher visual acuity than most licensing agencies require for drivers of private vehicles.

Visual Fields.—Second in importance to visual acuity are visual fields, i. e., form fields. These are obviously important for safe driving, for a driver must of necessity possess some depth and lateral perspective in the horizontal meridian in order to pass approaching vehicles safely as well as being aware of approaching vehicles or pedestrians from the side.

Patients with visual form fields of 140 degrees or more may be advised that this field is sufficient for the task of operating a motor vehicle. Patients with form fields less than 110 degrees should be advised not to drive. The patient with a field between these limits must be evaluated on the basis of the conditions under which he drives and the amount of lateral vision he possesses.

Individuals with markedly constricted fields, such as those suffering from severe glaucoma or retinitis pigmentosa with peripheral blindness, are unfit for safe driving and should be advised not to drive.

Ocular Muscle Imbalance.—The accident potential of ocular muscle imbalance is indirect through causing driver fatigue. However, when diplopia occurs, accidents are directly attributable to the diplopia. Therefore, all patients with uncontrolled diplopia should be advised not to drive a motor vehicle.

Color Blindness.—Color blindness has in the past been considered to be a potential cause of highway accidents. At the present time, however, traffic lights have been standardized, and, except in cases of those engaged in interstate or heavy transport, it is doubtful if color blindness or deficiency is of any great consequence.

Dark Adaptation.—Dark adaptation and susceptibility to glare are of importance in night driving, but at the present time no valid data are available as to their importance in the causation of highway accidents. Of course, dark glasses should not be worn for night driving and windshield tinting should be limited to the upper one-third.

Depth Perception.—Tests for depth perception are inadequate at this time. The road test is still best and is practical.

Otolaryngology

Deafness and dizziness or vertigo due to internal or middle ear disturbances are the principal otological symptoms of significance in the safe operation of a motor vehicle.

Although deafness is a handicap in the safe operation of a motor vehicle, usually it is compensated for quite well. The deaf driver, being fully conscious of his disability, tends to be cautious and fully alert at all times. Moreover, the use of an outside rear view mirror is of great value. The wearing of hearing aids has not proved practical in noisy commercial or passenger transport vehicles. However, in the operation of private vehicles, patients who successfully wear hearing aids frequently find the hearing aid most useful. Thus, much depends on the vehicle, road noise, the patient, and his type of deafness. Although deafness is disqualifying in the operation of a passenger transport vehicle, this is not necessarily so for the operation of a commercial or private vehicle. However, some licensing authorities and the Interstate Commerce Commission have specific regulations in this matter which the physician will need to consult when patients need advice in this area. This information may be secured from the state licensing authority.

Patients subject to attack of Ménière's syndrome or sudden dizziness, no matter what the cause, should be advised not to operate a motor vehicle until proper treatment has controlled such attacks, when he may resume driving a private vehicle but not a commercial or passenger transport vehicle. The character of the attacks may change so there is sufficient warning of the impending attack enabling the patient to drive his vehicle over to the curb or off the highway. In such an event the patient may resume driving a private vehicle.

There are very few laryngological conditions which interfere with the safe operation of a motor vehicle. However, individuals with seriously handicapping speech disorders or any irremedial deformities or diseases of the mouth, nose, and throat interfering with feeding, speech, or breathing should not operate a passenger transport or commercial vehicle. Patients with a tracheotomy should not drive a motor vehicle because of the possibility of sudden obstruction of the tracheotomy.

Surgery and Orthopedics

The role of acute surgical lesions as causes of traffic accidents is slight, for an individual so afflicted is unlikely to be driving. Chronic disabling surgical lesions, in those still able to drive, are apt to be compensated for and are not significant causes of traffic accidents. Of chief concern surgically are the severe injuries sustained by occupants of motor vehicles involved in accidents and how such severe injuries can be reduced through such means as car design, seat belts, and crash helmets. These problems are beyond the scope of this guide.

Many orthopedic handicaps may interfere with safe driving. A guide to aid physicians in evaluating such handicaps is available.[1] It is important to remember that the final acts of driving, however complicated the psychosomatic-mechanical reaction involved, are dependent on the biomechanical efficiency of the bones, joints, and muscles. Moreover, orthopedic aspects overlap other essential abilities for safe driving—for example, the effects of spinal immobility, in limiting the peripheral field of vision, which is so important, particularly at intersections.

The patient must be in such physical condition that he can control a motor vehicle with safety. This means he must have sufficient strength to control the vehicle; turn the steering wheel, and apply the brakes sufficiently to "slide the wheels." He must be able to reach all controls required in the operation of the vehicle, whether by mechanical means on the vehicle or by suitable prosthetic devices. Moreover, those so handicapped must demonstrate that they can successfully operate their vehicles in this manner.

Experience has shown that orthopedically handicapped persons do not as a rule meet with accidents more often than those not so afflicted. It is known that the handicapped person instinctively is more alert to danger and exercises more caution in driving. Ease of muscular fatigue in these individuals needs to be appreciated, but, again, most of these handicapped individuals are accustomed to regulating their energies and avoiding disabling fatigue.

Specific Requirements.—Specific requirements in persons are best considered from the standpoint of body regions as they relate to the static and dynamic demands upon the driver of a motor vehicle. Moreover, shifting of the line of gravity in the seated posture effects efficiency, comfort, and ability of driver performance, particularly in the orthopedically handicapped. All assessments with respect to driver performance must take cognizance of the variance in the center of gravity through the body of the driver and its effects upon the functional capacity of body parts.

Head and Neck Movements.—Relationships and mobility should be normal for operators of commercial and passenger transport vehicles. Variable degrees of restricted movements of the head and neck are compatible with safe operation of private vehicles.

Any limitation of rotation of the head by 50% or more by disease or splinting necessitates compensatory aids to enable these individuals to drive safely. Outside mirrors and swivel type bucket seats can sufficiently aid some of these people. In case of accident, especially when treatment is supplemented by any kind of supportive splinting or

bracing, such individuals may be more vulnerable to injury and should be so advised by their physicians. Patients wearing a neck cast or brace should be advised not to drive until recovery has progressed to the point where pain and cervical restrictions of movement are minimal and external support is no longer necessary.

The patient with spastic torticollis should be advised not to drive a motor vehicle. Patients with mild congenital torticollis without pain or significant disability may be advised that it is safe for them to drive.

Thoracic Region of the Spine.—Patients with disabling diseases and deficiencies of the thoracic region of the spine should be advised against driving a commercial or passenger transport vehicle. Many compromises are possible with regard to private vehicles. Patients with arthritis and older injuries if associated with marked deformity or painful restrictions of motion or respiratory excursions should be advised not to drive a motor vehicle. However, proper bucket type swivel seating with restraining seat belt may provide sufficient compensation for some of these individuals. Patients with interscapular pain which causes restriction of motion of the shoulder joint and increases vulnerability to fatigue and irritability should be advised not to drive until they recover.

Mild to moderate degrees of scoliosis do not ordinarily interfere with safe driving. However, patients with severe grades of scoliosis, when it is accompanied by painful arthritis or ease of fatigue, should be advised not to drive a motor vehicle. The scoliotic patient may be helped by seating of the bucket type or other seating specially tailored to his needs, or possibly with the aid of a brace. However, those wearing braces should be carefully evaluated by the physician as to their ability to manipulate a motor vehicle safely. Individuals with extensions under the arms which could interfere with axillary circulation frequently are too incapacitated to drive safely.

Patients with osteoporosis are vulnerable to vertebral fractures from abrupt deceleration and should be so warned. Such patients can be safeguarded by bucket type seating and proper safety restraint, particularly shoulder harnesses and seat belts. With these aids they may be advised that it is safe to drive. Patients with myeloma of ribs and spine should be advised in a similar fashion.

Lumbar Region of the Spine.—The seated position imposes rather unusual stresses and strains on the lumbar region of the spine. These stresses may induce fatigue accompanied by irritability. The seated position calls for a certain amount of compensatory flattening of the normal lordotic curve, which is influenced to some extent by proper mobility in the hip joints. Stiffness of the hip joints puts added strain on the lumbosacral junction and additional flexion forces during abrupt forward decelerations thus making the lumbar vertebrae more vulnerable to compressive fractures. Patients with a stiff hip should be warned of this danger and encouraged to seek seating revisions and shoulder type harness and safety belt restraints for their own safety.

The lumbar region of the spine should be normal for drivers of passenger transport and commercial vehicles. Lumbar abnormality may not incapacitate an individual from safely operating a private vehicle.

Many patients with lumbar deformities, stiffness, and neuromuscular deficits from cord or nerve root defects are not fully competent to operate a motor vehicle under all conditions. Such patients should be advised appropriately to restrict their driving. Although arthritis, osteoporosis, congenital anomalies, and scoliosis commonly are disabling, power steering, power brakes, and semiautomatic transmission are helpful to most of these individuals, enabling them to drive a private vehicle with safety.

Patients with herniated lumbar disks with much pain should be advised against driving, particularly during acute attacks.

Upper Extremities.—Normal functions are required for drivers of passenger transport and commercial vehicles. A one-armed person, provided the one arm is a good one, can operate a private vehicle safely, especially one equipped with power steering and a wheel button. The same is true for the loss of one arm and one leg, which requires the balancing effects of proper protheses.

Hands on the wheel of an automobile, in addition to serving to balance the driver, also are helpful in bracing against rapid deceleration. Obviously, the grasping power of the hands is of basic importance. An adequate number of opposing digits to the thumb are essential for proper gripping. Each individual with impairment of hand function needs to demonstrate sufficient ability to operate properly his private motor vehicle. Power steering is of great assistance to many individuals so handicapped.

Lower Extremities.—Normal function is essential for drivers of passenger transport and commercial vehicles. However, with good arms, even absence of both legs may not prevent the safe driving of a private vehicle with proper protheses and perhaps special hand controls. During prolonged driving, fatigue will accrue from improper buttock and thigh support. Ankylosis of the hip, as it relates to low back disability, has been discussed already.

Deformities of the feet or legs which require special shoes or braces may also require special controls on the vehicle. The foot controls must be spaced far enough apart to avoid pressure on the accelerator when the brake is being sought.

Stability of Joints.—Stability of joints as well as mobility and strength should be evaluated in reaction to driving ability.

Neurological, Emotional, and Psychiatric Disorders

The unhospitalized patient with an emotional, neurological, or psychiatric disorder presents the conscientious physician with a difficult problem. The disability by its very nature may create a special hazard in the safe operation of a motor vehicle. Yet frequently there are strong socio-economic justifications for the patient continuing to drive.

Inasmuch as several states have in recent years established special procedures for licensing individuals with certain neurologic and psychiatric disorders, physicians should secure copies of these laws and regulations from the state licensing authority and acquaint themselves with the procedures in order properly to advise their patients.

Neurological Disorders.—Convulsive disorders, including major or minor seizures, petit mal, or psychomotor epilepsy are the most frequently encountered neurological disorders impairing driving ability.

Epilepsy: Epileptic patients not receiving medicaments and who have been seizure free for a minimum of two years are considered good risks for the operation of private vehicles but should be advised not to drive a commercial or passenger transport vehicle. Such patients should be advised not to consume alcoholic beverages in any form for at least 24 hours prior to driving. Moreover, fatigue should be avoided and six hours should be the maximum number of hours behind the wheel in one day. Also, epileptic patients should be advised that night driving may be particularly dangerous because the photic stimuli from opposing headlights may precipitate a seizure. Emotional stress should be minimized by avoiding driving in peak traffic hours. These patients should be advised to secure a review of their progress and physical condition at least twice a year by a physician. Epileptic patients under medication should be advised not to drive a motor vehicle until they have been seizure free for a minimum of two years, and then they should drive only private motor vehicles. They should be advised to limit their driving to daytime and avoid rush hours. They represent a risk not only because of the likelihood of a seizure suddenly occurring while driving but, in addition, the medications may produce undesirable side-effects which interfere with driving capabilities.

Faintness, Syncope, and Episodic Weakness: It would be impossible to cover all the syndromes, diseases, or physiological disorders which produce these symptoms. It is important, therefore, that the pattern of these symptoms be evaluated carefully in terms of impairment of driving ability. The isolated occurrence probably is of little concern. Patients having a history of multiple occurrences should be advised not to drive a motor vehicle until a diagnosis can be established and satisfactory corrective measures have been instituted. In instances in which no diagnosis can be made and symptomatic therapy is not effective, the patient should be advised not to drive a motor vehicle.

Narcolepsy: Narcolepsy is rare and infrequently encountered. Its onset is usually during adolescence or adult years and its etiology is poorly understood. The treatment is symptomatic. Patients under treatment should be advised not to drive a motor vehicle until they have been symptom free for two years and are experiencing no adverse side-effects from medicaments. If it becomes desirable to discontinue treatment, such patients should be advised not to drive for two years. If there is no recurrence of symptoms, they may resume unlimited driving.

Disorders Affecting Muscular Control or Coordination: Paralysis agitans, poliomyelitis, hereditary chronic progressive chorea with mental deterioration (Huntington's chorea), multiple sclerosis, hereditary sclerosis, spinal form (Friedreich's ataxia), syringomyelia, muscular dystrophy, cerebral palsy, myasthenia gravis, tumors of the brain and spinal cord, cerebellar degenerative diseases, amyotrophic lateral sclerosis syndrome, post-traumatic syndromes, and intracranial suppurative processes affect muscular control and coordination. The foregoing list of diseases is not complete but suggests the wide variety of processes affecting the nervous system. Each of these will pose special problems with respect to the driving abilities of the individual patient.

The more serious disorders generally cause either rapid deterioration or sufficient functional disability of such degree that the patient will of his own volition cease driving. In those patients with more slowly progressing cases, when the disability reaches a point making driving unsafe, it is the physician's responsibility to recommend to the patient that he discontinue driving.

Mental Deficiency: Patients with an intelligence quotient below 70 and many borderline mentally defectives with an intelligence quotient between 70 and 80 are more susceptible to accidents than normal individuals when faced with emergency situations requiring accurate judgment or decisive action. Patients with intelligence quotients below 70 should be advised not to drive their private vehicles in rush hours, in congested traffic, or under other stress traffic conditions. These individuals also should be advised not to drive commercial or passenger transport vehicles.

Emotional Disturbances.—Many varied stresses and situations create in normal individuals a temporary emotional upset impairing their driving ability. The manifestations occur in three abnormal behavioral patterns. First, the individual is so absorbed in his problem that he is indifferent and inattentive to traffic and the world about him. Second, some individuals become greatly despond-

ent, with actual depression and psychomotor retardation. Such individuals have sufficiently slowed reflexes to make driving a real hazard. Third, many such individuals become antagonistic, impulsive, or openly aggressive with loss of judgment and loss of sense of caution. Patients exhibiting any of these three types of symptoms should be advised not to drive a motor vehicle until they have recovered.

Some patients live under more or less permanent emotional stress. Until, with help and understanding, such patients have worked out an adequate adjustment to the situation, they should be advised not to drive a motor vehicle. Most patients under temporary or persistent emotional stresses producing either aggressive or depressive reactions are unaware of the increased likelihood of an accident. Such patients need to be made fully cognizant of the increased dangers inherent in their situation while being helped to work out a satisfactory solution.

As yet, only limited reliable data are available to aid in identifying drivers most likely to become involved in accidents. The characteristics most clearly related to repeated accidents or high accident rates are very low intelligence, youthfulness, and a personality make-up featured by egocentricity, aggressiveness, antisocial trends, and social irresponsibility.

Psychiatric Disturbances.—The psychoses, affective reactions, schizophrenic reactions, and paranoid reactions in the majority of patients present no recognizable morphologic changes, but the functional disability may be severe. In the majority of instances the frankly psychotic patient will be under hospital care and incapable of driving a motor vehicle. After hospitalization there are in many states special provisions for relicensing these individuals. Physicians should be familiar with these regulations. In exceptional instances where a frankly psychotic patient is being treated on an outpatient basis, the patient and a responsible member of the patient's family should be advised that the patient should not operate a motor vehicle.

Patients who have been returned to the community and require maintenance therapy with the ataractic drugs should be advised not to drive a motor vehicle if drowsiness or syncope occurs. Patients receiving maintenance therapy with the tranquilizers should be observed closely for possible deleterious side-effects from alcohol. Such effects have been reported with certain of the tranquilizer drugs.

Anxiety reactions, dissociation reactions, conversion reactions, phobic reactions, obsessive-compulsive reactions, and depressive reactions are among the conditions observed in the psychoneurotic patient. The patient with a psychoneurosis represents an unknown factor with respect to highway safety. Each case requires separate evaluation regarding alertness, social behavior, and possible psychomotor retardation. If no significant behavioral problem or drug therapy side-reaction exists, then the psychoneurotic patients may be advised that it is safe for them to drive. Careful appraisal, although often difficult, of the driving capacities of all these patients, with sound advice and recommendations to them, provides the physician with an exceptional opportunity for protecting both the safety of his patients and the public. In this manner physicians can make most significant contributions to the prevention of highway accidents.

Alcohol

Alcohol is the responsible factor in a large percentage of the motor vehicle accidents attributed to speed, reckless driving, and driving on the wrong side of the road. Detailed studies in selected areas show that approximately 50% of the fatal accidents involve a drinking driver. If this 50% figure holds nationally, then, in 1958, about 15,000 people died in accidents involving a drinking driver. Although valid data are not available, there is no doubt that many of the accidents which caused injury to about 5,000,000 people in 1958 involved a drinking driver. This situation urgently needs medical consideration.

Pharmacology.—Ethyl alcohol (i. e., grain alcohol, C_2H_5OH) is a central nervous system depressant, even though for years it was called a stimulant. Its effect on human beings is in all phases and stages a depressant. While many individuals will have a sense of exhilaration after consuming alcohol, this is not due to stimulation but to a depression of the inhibitory mechanism. The more recently acquired inhibitions are the first to be affected. Studies reveal that test subjects after consumption of alcohol almost unanimously believe that their performance is unimpaired or even better than usual, whereas objective testing demonstrates that performance is impaired. This, too, is evidence of a depressant action of alcohol—a depression of the critical sense. This depressant action of even small doses of alcohol is of obvious importance in the operation of motor vehicles.

Alcohol and Driving Ability.—Holcomb concluded from his studies that driving performance began to be impaired at a blood alcohol level of 0.05%, or 50 mg. per 100 ml. of blood. Lauer revealed that driving performance in many persons is impaired at an even lower level, 0.035%, and emphasized the importance, at this low level, of such factors as the impairment of judgment, observation, tolerance to glare, and sense of caution, even though muscular performance was not affected.

In 1950 the definitive study by Bjerver and Goldberg appeared and confirmed once again that "the role that alcohol plays in causing traffic accidents is probably considerably greater than appears from official statistics." They ascertained the average threshold of impairment of driving ability in expert drivers, accustomed to consuming moderate amounts of alcohol, as 0.035 to 0.040% alcohol in the blood.

Studies by Smith and Popham of the drivers involved in personal-injury motor vehicle accidents indicate that driving impairment begins at a blood alcohol level of 0.03%. Loomis and West reported in 1959 that "some impairment of ability to perform a simulated driving test could be detected in some individuals when the blood alcohol concentration was as low as 0.03%."

Alcohol Consumption and Blood Alcohol Level.—Almost everyone is interested in the practical aspect of how much liquor of one kind or another can be imbibed before reaching a blood alcohol level considered dangerous for driving. Numerous studies, using individuals accustomed to drinking, all are in full agreement that two 12-oz. bottles of 3.2% beer or 2 oz. of 100 proof whisky consumed within one hour will put the average moderate drinker in the zone of impaired driving ability, i. e., with over 0.035% alcohol in the blood. Three 12-oz. bottles of beer or 3 oz. of whisky will result in more that 0.05% alcohol in the blood of this same individual.

Rate of Oxidation and Elimination.—As the drinker is adding alcohol, the organism is oxidizing it in the liver and eliminating it through the kidneys and the lungs. The concentration of alcohol in the exhaled breath is proportional to the concentration of alcohol in the blood which is circulating through the lungs in a ratio of 2,100:1. The average person of 150 lb. (68 kg.) can oxidize and eliminate about one-third fluid ounce of alcohol per hour, decreasing the concentration of alcohol in his blood by approximately 0.015% per hour. Two hours will reduce the blood alcohol concentration about 0.03% if the individual does not consume more alcohol. This offers a clue to length of the necessary waiting period after drinking before driving.

Measurement of Blood Alcohol Levels.—While direct chemical measurement of the alcohol in the blood is probably the most accurate, the most convenient method is measuring the alcohol in the breath. Several excellent breath testing devices have come into being and are relied upon more and more since the breath alcohol quite accurately reflects the alcohol level of the blood circulating through the lung.

Physician's Advice on Drinking and Driving.—It is not important whether the blood alcohol level is determined on an ascending or descending curve of intoxication; also, the kind of alcoholic beverage consumed, the rapidity of its consumption, or whether it was consumed on a full or fasting stomach is not of material significance. Whether the individual is an experienced drinker with a high degree of tolerance or one who seldom drinks is not the important point. The only significant fact is the amount of alcohol in the individual's blood and the consequent impairment of his driving ability.

The average individual with a blood alcohol level of 0.05% or higher suffers significant deterioration of his driving skill and is a potential menace on the highway. What then, can practicing physicians do to prevent these thousands of deaths and injuries each year? First, patients must learn the basic facts of alcohol consumption and motor vehicle operation. One drink may be tolerated. Two drinks put one in the level of impairment for about two hours. Three drinks are too many.

Summary

The Committee on Medical Aspects of Automobile Injuries and Deaths has compiled in this guide a summary of the pertinent medical data presently available concerning the ability of an individual to operate a motor vehicle safely. Much research remains to be done on factors such as physical disabilities, certain physiological states, and drugs, in connection with safe driving ability. However, on the basis of present knowledge, it is believed that a conscientious medical evaluation of the individual's fitness to drive safely, with appropriate follow-up, can reduce motor vehicle accidents very significantly.

References

1. Guide to Evaluation of Permanent Impairment of Extremities and Back, by Committee on Medical Rating of Physical Impairment, J. A. M. A. (special edition) Feb. 15, 1958.

STATEMENT ON THE DOCTOR-DRAFT ACT

February 2, 1959

Honorable Carl Vinson, Chairman
Committee on Armed Services
U. S. House of Representatives
Washington 25, D. C.

Dear Chairman Vinson:

The purpose of this letter is to submit for the consideration of the Committee on Armed Services the position of the American Medical Association on H. R. 2260, 86th Congress, a bill, which, in part, would extend until July 1, 1963, the induction provisions of the Universal Military Training and Service Act.

With respect to the extension of the special provisions of this Act applicable to medical, dental, or allied specialists, the American Medical Association wishes to reaffirm its position which was outlined in testimony presented in May, 1957, before the House Armed Services Committee on the bill which subsequently was enacted as Public Law 85-62, approved June 27, 1957. At that time, the Association testified that "if the demands for the defense and security of our nation are such that, in the opinion of Congress, it is necessary to have a draft act to maintain the strength of our Armed Forces, then the extension of the present legislation would be one method to insure sufficient physicians for the military services."

The Association also recommended retention of the provisions of the law relating to the national, state, and local committees which advise the Selec-

tive Service System in regard to the selection of medical, dental, and allied specialists required by the services. These advisory committees consider, among other factors, the needs of the civilian population in the communities from which these physicians would be taken. The Association is pleased that this provision is a part of the current law.

In regard to specialist categories, the Association recommends, as it did previously in May, 1957, that the word "other" should be substituted for the word "allied" in this section of the law. This would authorize a selective call for other specialists, such as engineers, physicists, other scientists, etc., which might be needed by the military forces. Presently, the law provides only for the selective call-up of medical, dental, or "allied" specialists.

The Association believes that physicians should be registered and classified in the same manner as other citizens in the same age group, deferred for educational purposes in the same manner as other registrants, and called to active duty or inducted under the same general provisions as other registrants deferred for educational purposes.

It is noted that the pending bill proposes a four-year rather than a two-year extension of the Universal Military Training and Service Act. We believe this additional extension of time should be fully explained and justified to the Committee. We believe that this justification is necessary because scientific and technological advances have resulted in rapidly changing concepts of military manpower requirements. Consequently, there has resulted, directly or indirectly, current and projected reductions in the strength of the Armed Forces. It is conceivable that future manpower requirements may be subject to further downward revisions. A lesser period of extension of the law would permit a timely review of military manpower requirements in light of pertinent changes in the then current military situations. The Association believes that this would be particularly desirable with respect to the call-up of medical and allied specialists because of the increasing demands and requirements of the civilian population for the nation's medical and health resources.

As you know from our previous appearances before your Committee, the Association has had a keen and sustained interest in military medicine for many years. Through the Surgeons General of the military services, we have maintained a friendly and close working arrangement in the consideration and advancement of military medical affairs. We feel that the health of the nation requires a careful correlation of military and civilian medicine. In furtherance of this objective, the Association, working with the military services, has attempted to insure improvement in the utilization of medical manpower by the Armed Services and a strengthening of the career incentive program for medical officers.

On behalf of the American Medical Association, I would like to thank you for this opportunity to present our views on H. R. 2260 and to assure your Committee of our willingness to continue our assistance in providing the members of the military services with the finest medical care.

Yours sincerely,
F. J. L. Blasingame, M.D.

STATEMENT ON PROPRIETARY NURSING HOMES

January 26, 1959

Senator John J. Sparkman, Chairman
Subcommittee on Housing
Senate Banking and Currency Committee
Senate Office Building
Washington 25, D. C.

Dear Senator Sparkman:

I am writing this letter to you to express the official views of the American Medical Association with respect to Title II of S. 57, 86th Congress, which I understand, is now pending before your Committee. Our position with respect to this proposal, which would make proprietary nursing homes eligible for mortgage insurance, is one of active support.

Our deep interest in the subject of the health care of the aged and the occurrence of some significant recent developments have prompted me to mention certain activities in this field before outlining the specific reasons for our support of Title II of S. 57.

Since its beginning, more than a century ago, the American Medical Association has been deeply concerned with the medical aspects of caring for the aged. In recent years, however, our interest and activities in this connection have kept pace with the ever-increasing amount of national attention being given to the subject both within the government and among groups and associations outside government. This general trend is understandable, of course, since the proportion of our population over age 65 is increasing at an amazing rate. In 1900 there were only three million of these elderly citizens whereas now there are approximately fifteen million.

For the past several years the American Medical Association has had a Committee on Aging, composed of some of the leading medical authorities in the United States in this field, which has devoted its full effort to this problem. In addition there are forty-five Committees on Aging actively at work in the State medical societies. To facilitate and coordinate the work of these committees, a set of guides for their organization and operation has been developed and made available to them.

As a climax to a series of five regional meetings which were held last year, and in an effort to prepare a positive program for use by the state com-

mittees, an A. M. A. National Planning Conference for Medical Society Action in the Field of Aging was held in Chicago on Sept. 13-14, 1958. This Conference was attended by over 175 people including official state medical society representatives from 46 states and the District of Columbia, as well as 27 state health departments. A copy of the official proceedings of this Conference, together with a related brochure entitled "Health Aspects of Aging" are enclosed for the information of the Committee.

In our consideration of the health problems of the aged we have also given serious thought to effective methods of financing medical and hospital care. In considering this facet of the problem, it should be noted that enrollment of older people under voluntary health insurance has increased substantially in recent years. In the last several years alone the percentage of coverage has gone up approximately one hundred per cent. Presently, exclusive of the approximately three million older persons who receive public assistance, more than fifty per cent of those over age 65 have some form of health insurance. Nevertheless, in our opinion, there is a need for further expansion of voluntary health insurance coverage among the aged.

During the last year the Association has conducted or participated in numerous meetings and conferences with commercial insurance carriers and with state and national Blue Cross and Blue Shield Commissions to encourage still greater efforts in the development of new insurance programs and in the expansion of lower cost protection for persons over age 65. These companies, as well as Blue Cross and Blue Shield plans, are now engaged in intensive studies designed to develop new types of policies tailored to meet the needs of the aged ill; present retirement financing of health insurance policies with paid-up status at age 65; use of life insurance after 65 to pay for health care; and the application of deductible and co-insurance to permit coverage of costly illnesses at a low premium rate, among others.

In order to stimulate further the interest of state medical societies and individual physicians in this movement the House of Delegates of the Association approved the following resolution at its Clinical Meeting which was held in Minneapolis in December of 1958:

> For persons over 65 years of age with reduced incomes and very modest resources, it is necessary immediately to develop further the voluntary health insurance or prepayment plans in a way that would be acceptable both to the recipients and the medical profession. The medical profession must continue to assert its leadership and responsibility for assuring adequate medical care for this group of our citizens.
>
> Therefore, the Council on Medical Service recommends to the House of Delegates the adoption of the following proposal:
>
> That the American Medical Association, the constituent and component medical societies, as well as physicians everywhere, expedite the development of an effective voluntary health insurance or prepayment program for the group over 65 with modest resources or low family income; that physicians agree to accept a level of compensation for medical services rendered to this group, which will permit the development of such insurance and prepayment plans at a reduced premium rate.
>
> This recommendation has been studied and restudied by the Board of Trustees and has received its wholehearted endorsement.

In addition to the numerous and varied medical, scientific and socioeconomic activities being pursued in this field, physicians through their associations have, for some time, recognized the need for additional organizational weapons to attack these problems. For many years the American Medical Association was an active participant in the affairs of the Commission on Chronic Illness, in cooperation with representatives of the general public, industry, labor, agriculture, education, religion, social sciences, journalism, health, and welfare. One of a number of studies which were conducted was entitled "Nursing Homes, Their Patients and Their Care." A copy of this study which was published by the United States Public Health Service, is also attached for the information of your Committee.

Last year the American Medical Association joined with the American Hospital Association, the American Dental Association, and the American Nursing Home Association in the formation of The Joint Council to Improve the Health Care of the Aged. In broad outline the program of the Joint Council will include a coordinated plan of research designed to (*a*) determine the extent, utilization, and availability of facilities and the economic status and resources of the aged; (*b*) spearhead the expansion and experimentation in all types of voluntary health insurance coverage for the aged; (*c*) encourage the expansion of health care facilities for the aged; (*d*) encourage the development of community health services for the aged; (*e*) urge state and local legislative bodies to provide realistic financial support for medical, hospital, and nursing home care of aged public assistance recipients; and (*f*) appraise the problems of the aged who are mentally ill and provide an intensification of education, research, and action programs directed toward health problems of the aged at national, state and local levels.

In its work in connection with the over-all medical care problems of the aged, the American Medical Association has long recognized the importance of proper nursing home facilities. For this reason the Association has had a close relationship for some time with the American Nursing Home Association to work toward the development of higher standards for medical care in nursing homes. In February of 1958 the first National Conference on Nursing Homes and Homes for the Aged was held in Washington. Our Association was an active participant at that meeting. On Dec. 16, 1958, a Conference on Nursing Homes and Related Facilities between representatives of our Association, the American Hospital Association, the American Nurs-

ing Homes Association, Public Health Service, and Public Assistance Agencies was held in Chicago to discuss current activities and projected programs concerning facilities for the chronically ill and the aged. The purpose of this meeting was to seek a coordinated effort on the part of interested national organizations.

In addition the A. M. A. is currently making a survey of nursing homes throughout the United States. The American Nursing Home Association is also engaged in such a project and is surveying approximately five thousand member homes to obtain data on the cost of care to the patient, the type of patient in the homes and the type of medical care provided.

As an outgrowth of all of these various related activities in connection with the health care of the aged, our Council on Medical Service has prepared a six-point program the details of which are outlined in the attached brochure entitled "Medicine's Blueprint for the New Era of Aging."

In conclusion I should like to comment more specifically with respect to the provisions of Title II of S. 57, 86th Congress. As stated at the outset, the American Medical Association has approved and supports a government-insured loan program of the FHA type for non-governmental hospitals and nursing homes whether their ownership is of a nonprofit or proprietary character.

We have taken this position because we believe there is a critical need for new and improved facilities tailored to the specific health requirements of older citizens. It is our understanding that representatives of other organizations such as the American Nursing Home Association have or will appear before your Committee. They have evidence accumulated over recent years showing that they cannot provide service of the desired quality or quantity because they are unable to obtain the credit they need on reasonable terms to permit them to increase the number and size of adequate nursing home facilities.

Under the Hill-Burton program the federal government has for years been assisting public and nonprofit institutions through money grants. It is also our understanding that the Federal Housing Administration is presently offering mortgage insurance for construction of large nonprofit institutional-type homes for the aged which may have a section for those needing nursing care. In our opinion the immediate need is for a similar program of loan guarantees for proprietary organizations, since according to the latest statistics over seventy per cent of nursing home patients are cared for in such facilities.

In the administration of a grant program under the Hill-Burton system and a loan guarantee program under the Federal Housing Administration, we recognize the desirability of cooperation; however, we believe that the loan guarantee program proposed under Title II of the pending bill should be administered by the Federal Housing Administration without mandatory supervision or coordination with the Department of Health, Education, and Welfare.

I would like to request that this letter and attachments, to the extent possible, be made a part of the record of the hearings of your Committee. If you or any of the members of the Committee desire additional copies of the attached material or any further information from our Association, we shall be happy to provide you with anything we have.

Your willingness to permit the American Medical Association to present its views on the pending proposal is sincerely appreciated.

Very truly yours,
F. J. L. Blasingame, M.D.

HEALTH INSURANCE FOR PERSONS OVER 65 YEARS OF AGE

The action of the House of Delegates at its 1958 Clinical Session (Dec. 2-4) adopting a supplementary report of the Council on Medical Service urging the development of special medical care coverage at low premium rates for persons over age 65 brought an immediate response from Donald H. Stubbs, M.D., chairman of the board of directors of Blue Shield Medical Care Plans, the national association of Blue Shield plans.

Dr. Stubbs' announcement stated "Physicians everywhere have been urged to support this proposal and it is especially significant to the 120,000 doctors who are now participating in Blue Shield Plans, because they recognize their civic duty to help provide medical care to their patients under nonprofit programs with local control."

Dr. Stubbs said he believed local Blue Shield plans are ideally equipped to assist the medical profession in developing low cost coverage for senior citizens because each plan is operated under local medical society sponsorship in the area it serves and can put into effect any program to meet the exact specifications of coverage for elder citizens which physicians believe to be desirable. He also pointed out that the plans can be especially helpful in developing low cost coverage under their regular programs to some 2,500,000 subscribers over 65 years of age who have either been enrolled under Blue Shield group programs which ordinarily impose no age limits or who have joined Blue Shield before reaching 65 and have elected to continue their coverage on retirement.

The A. M. A. proposal, according to Dr. Stubbs, calls for a program under which physicians would accept a level of fees related to the modest resources and income of persons over 65 years of age. Such an arrangement, he indicated, would make it possible to provide the coverage at low rates and constitute a program that persons living on retirement incomes could easily afford.

Prepared by the Council on Medical Service.

According to the Blue Shield release, Dr. Stubbs indicated that each of the 64 Blue Shield plans in the United States will be asked to go to work immediately with local medical groups to draft benefit schedules and rates for coverage . . . to meet the needs of persons past 65 years of age. He added that guidance and information would be offered local plans by the national Blue Shield association in Chicago to expedite their efforts in developing their contracts.

To draft suggested patterns of coverages, special committees of the Blue Shield Board were created with the following twofold objectives: 1. To develop a practical pattern of benefits designed to meet the special medical needs of persons over 65 years of age. 2. To suggest a level of medical compensation for those benefits which would permit rates commensurate with the "modest resources or low family income" of persons in this age category.

Certain obvious facts were recognized in approaching these objectives. According to these committees, utilization and cost studies clearly indicated that the incidence of medical care for this age group is greater and, consequently, costlier. But these studies also produced evidence that the problem is not as severe as had been anticipated. It was the conclusion of the committees that the provision of adequate in-hospital medical care benefits must be a part of any program offered to this segment of our population.

Those studies reportedly revealed that, although the incidence of surgery increases in certain categories, other high cost and high incidence procedures, such as tonsillectomies, appendectomies, etc., common in the younger age group, can be minimized. It was the consensus that preexisting conditions will have to be covered after a reasonable (six months) waiting period.

After thorough consideration of these and other factors, the Blue Shield committees recommended that the following benefits be provided with reasonable premium rates to those over 65 years of age with "modest resources or low family income": (*a*) surgery; (*b*) anesthesia; (*c*) in-hospital medical care for 120 days; (*d*) diagnostic x-ray in the hospital, in the hospital outpatient department or doctor's office if hospitalization follows; and (*e*) radiation therapy.

During the course of preparation of the suggested programs, representatives of the Blue Shield staff conferred on two occasions with the Committee on Insurance and Prepayment Plans of the Council on Medical Service seeking its counsel and assistance.

On Jan. 26 the national Blue Shield office submitted the proposal to the local member plans. Subsequently, the Council on Medical Service directed the following memorandum to those constituent associations and component societies sponsoring or approving Blue Shield plans:

As all of us know, there is a widespread interest in the problems of the so-called senior citizens. This includes problems concerned with health care, as well as the financing of such care. And, since voluntary health insurance is a primary means of financing health care, it is logical that the medical profession should look to insurance or prepayment programs to assist in meeting this new problem.

Recognizing this, the House of Delegates, at its Minneopolis Session (December, 1958), adopted a report urging the development of special insurance and prepayment programs for persons over 65 with "modest resources and low family income." A copy of this report and the comments of the Reference Committee are enclosed for your information.

As a step in implementing this report, the Committee on Insurance and Prepayment Plans of the Council on Medical Service conferred with representatives of Blue Shield to discuss the types of benefits that might be included in a program for those over 65. As a result, Blue Shield has set forth its suggestions for such coverage in the enclosed Policy Letter to its member plans. The Committee agreed in general with these proposals. It has, however, one important addition which it believes should also be considered. A major effort must be made to provide an alternative to hospitalization. It was agreed by the Committee that every effort should be made to provide for a specified number of office and home calls per year. Such a provision should also permit payment for calls to nursing homes as an alternative to hospitalization.

With this addition, and in full recognition that income ceilings and physicians' fees for any program must be viewed in the light of local or state conditions, the Committee recommends that your medical society give earnest consideration to implementing programs set forth by Blue Shield and other groups, which would carry out the intent of the House of Delegates' action.

It is the Committee's hope that the medical societies will initiate meetings to discuss this problem. The Committee would also appreciate being informed of any developments that may occur so that the House of Delegates, the Board of Trustees, and the Council on Medical Service may be aware of the progress being made.

The active interest of the private insurance companies is evident from the report of a special meeting of the Health Insurance Association of America held in New York City, Dec. 8, 1958. At that meeting a resolution was approved setting forth principles designed among other things to promote more rapid spread of hospital, medical, and surgical insurance among people aged 65 and over.

Principal features of the resolution are that insurers offering individual coverage (*a*) should continue and accelerate their progress in minimizing the refusal of renewal solely because of deterioration of health after issuance, (*b*) should promptly make available to insurable adults policies which are guaranteed renewable for life, (*c*) should encourage sale of permanent health care insurance where the need for this type of coverage exists, and (*d*) should promptly take steps if they are not presently doing so to offer insurance coverage to persons now over age 65. Insurers writing coverage on a group basis, the resolution added, should (*a*) aggressively promote soundly financed coverages that will continue after retirement and (*b*) encourage the inclusion in group contracts of the right to convert to an individual contract on termination of employment.

MEDICAL NEWS

ALABAMA

Change of Address.—The Medical Association of the State of Alabama announced that subsequent to Feb. 20 all mail for the association should be directed to the following address: The Medical Association of the State of Alabama, 19 S. Jackson St., Montgomery 4, Ala.

Personal.—Richard T. Eastwood, Ph.D., was appointed executive director of university affairs for the University of Alabama Medical Center, Birmingham, effective Oct. 15.——Dr. Durward L. Lovell was appointed director of medical education, Birmingham Baptist Hospitals, Birmingham. He will be responsible for directing the hospitals' intern training program.

ARKANSAS

Dr. Dinning Named Head of Biochemistry Department.—James S. Dinning, Ph.D., associate professor of biochemistry, University of Arkansas Medical Center, Little Rock, was promoted to professor and head of the department of biochemistry to succeed Paul L. Day, Ph.D. Dr. Day resigned recently to become the first scientific director of the United States Food and Drug Administration. Dr. Dinning joined the university faculty in September, 1948, as an assistant professor and left in 1952 to spend one year at the University of Pittsburgh. He is a special consultant to the United States Public Health Service's Metabolism and Nutrition Study Section and this year closed out a five-year term as associate editor of *Nutrition Review*. He is on the editorial board of the *Journal of Nutrition* and is secretary of the Southwest Section of the Society for Experimental Biology and Medicine.

CALIFORNIA

Center for Cardiovascular-Renal Diseases.—A center for intensive treatment of cardiovascular-renal diseases and electrolyte problems was established and is in operation at Saint Joseph Hospital, Burbank. The center is in readiness to receive patients with cardiac or renal failure who may benefit from use of an artificial kidney, "medical" heart-lung machine, or with use of modern physiological monitoring equipment. The center is headed by Dr. Peter F. Salisbury.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

University News.—Dr. G. Meyer-Schwickerath, of the University of Bonn, spoke Nov. 14 at the Stanford University School of Medicine on "Treatment of Retinal Lesions and Intra-Ocular Tumors with the Light Coagulator." Dr. Meyer-Schwickerath's lecture was part of a four-day postgraduate conference on ophthalmology at the Medical School devoted to "The Causes of Failure in Intra-Ocular Surgery and Related Problems."

CONNECTICUT

Physiologist Wins International Award.—Dr. John F. Fulton, physiologist at the Yale School of Medicine, New Haven, was named 1958 recipient of the annual George Sarton medal of the History of Science Society, given annually for "outstanding contributions in history of science." Dr. Fulton is a former chairman of the department of physiology at Yale and now holds the rank of Sterling Professor of the History of Medicine. The George Sarton medal was created in honor of Dr. Sarton, Belgian scholar and professor of the history of science at Harvard, who died in 1956. Dr. Sarton founded the History of Science Society in 1912 and its publication, *Isis*, in 1912. The medal was created in 1955 and made possible by the Charles Pfizer Company. Dr. Sarton himself was the first recipient.

Personal.—Dr. David Seligson, formerly associate professor of clinical chemistry in medicine, University of Pennsylvania School of Medicine, Philadelphia, was appointed director of laboratories at Grace-New Haven Community Hospital and associate professor of medicine in the Yale University School of Medicine, New Haven.——The appointment of Dr. Morris A. Wessel, New Haven, to represent the Connecticut State Medical Society on the Governor's Committee on Children and Youth was announced. Dr. Harold M. Clarke, New Britain, was appointed to represent the society at a national conference on the medical care of veterans and their dependents.

FLORIDA

Society News.—The Board of Governors of the Florida Medical Association has announced the appointment of Mr. William Harold Parham as executive director.——The Greater Miami Eye, Ear, Nose and Throat Society, which meets quarterly in March, May, October, and December on Thursday evenings at the McAllister Hotel, Miami, has elected

the following officers for 1959: president, Dr. Mariano B. Caballero; vice-president, Dr. Joseph Freeman; secretary-treasurer, Dr. H. Carlton Howard.

HAWAII

Society News.—The following have been elected officers of The Honolulu Pediatric Society for 1959: president, Dr. Duke Cho Choy, Honolulu; recording secretary, Dr. Frances F. Nakamura, 1481 S. King St., Honolulu, Hawaii; corresponding secretary-treasurer, Dr. Calvin C. J. Sia, 1305 Kalakaua Ave., Honolulu, Hawaii.

IDAHO

Society News.—The newly elected officers of the Idaho Academy of General Practice are: president, Dr. Joseph G. Wilson, Moscow; president-elect, Dr. Arch T. Wigle, Pocatello; secretary-treasurer, Dr. Walter W. Wilson, Coeur d' Alene; A. A. G. P. delegates, Drs. Asael Tall, Rigby, and Ralph Buttermore, Grangeville; alternates, Drs. Aldon Tall, Rigby, and Louis F. Lesser, Boise.

ILLINOIS

Clinic for Juvenile Research at Jacksonville.—The State Department of Public Welfare announced Jan. 29 that its tax-supported Institute for Juvenile Research is opening a new regional medical clinic at the Infirmary in the Illinois School for Deaf to provide psychiatric, psychological and psychiatric social services to the emotionally disturbed child and his family for children under 18 years of age residing in Adams, Brown, Cass, Morgan, Pike, Schuyler, and Scott counties. Application forms may be secured from the Springfield regional office or local health departments. Address inquiries to the Institute for Juvenile Research, 404 State Office Bldg., Springfield.

Chicago

Dr. Sulzberger to Give Pusey Lecture.—The William Allen Pusey Lecture of the Chicago Dermatological Society will be given March 18, 7 p. m., at the Illini Union, 715 S. Wood St. Dr. Marion B. Sulzberger, chairman, department of dermatology and syphilology, New York Skin and Cancer Hospital and New York University Postgraduate Medical School and Hospital, will speak on "Some New Aspects on the Biology of the Skin." Preceding the lecture there will be dinner at the Illini Union at 6 p. m. (reservations $4.75 per plate). This is an open meeting and all physicians are invited to the dinner and lecture.

University News.—Dr. J. F. Tait, of the Medical Research Council of Middlesex Hospital Medical School, London, and The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., spoke on "The Secretion and Metabolism of Aldosterone in Normal and Pregnant Subjects" at The Chicago Medical School, Dec. 3.

Name Chairman of Surgery Department.—Dr. John L. Keeley was named professor and chairman of the department of surgery at Loyola University Stritch School of Medicine and head of surgery at Mercy Hospital, succeeding Dr. Harry A. Oberhelman, who will continue on the Mercy hospital staff as a member of the Loyola medical faculty. Dr. Keeley was one of the two American specialists called to Rome in 1958 to attend the late Samuel Cardinal Stritch, archbishop of Chicago. While in Rome he was named a Knight of Gregory of his late Holiness, Pope Pius XII, and Cardinal Stritch conferred the honor upon him. Dr. Keeley was an Arthur Tracy Cabot Fellow in surgery at Harvard in 1936 and 1937, and stayed at Harvard as the Harvey Cushing Fellow in surgery the following year. Dr. Oberhelman was chief of surgery at Loyola medical school and Mercy hospital for 17 years.

Hospital Plans Research Expansion.—Ten Chicago business leaders are launching a new board of governors of the Research Institute of Michael Reese Hospital & Medical Center, Mr. Irving B. Harris, president of the center, has announced. Purpose of the new board will be to "plan, program, and finance expansion of medical research." For the first time, Michael Reese reportedly will top one million dollars in research expenditures. About two-thirds of the funds for medical research at Michael Reese comes from governmental agencies, foundations, and such health organizations as the American Heart Association, the American Cancer Society, the American Fund for Psychiatry, the National Nephrosis Foundation, and the Damon Runyon Fund. Michael Reese's Medical Research Institute was founded in 1929, and now numbers 11 full-time departments and three affiliated laboratories.

KANSAS

Regional Physicians Meeting in Wichita.—The American College of Physicians, Kansas Region, will meet March 20 at the Allis Hotel, Wichita. Dr. Fred J. McEwen, of Wichita, is governor of the College for Kansas. Papers which include invited authors are:

Experiences with Cineangiography, Drs. Marvin I. Dunn, Thurl E. Andrews, and E. Grey Dimon, Kansas City.

Clinical Diagnosis of Ventricular Septal Defect, Dr. Alberto Benchimol, Kansas City.

Chronic Nonspecific Pericarditis with Effusion; Case Report, Drs. David Lukens, Calvin R. Openshaw, and Robert C. Tout, Hutchinson.

Milk Alkali Syndrome, Dr. Joseph Meek, Kansas City.
Liver Pathology Following Isoniazid (Marsilid) Toxicity, Dr. Charles G. Hermann, Topeka.

The sessions will close with a dinner (6:15) at which Dr. William C. Menninger, regent of the college, will be guest speaker, presenting "Brains Before Bricks." For information write the American College of Physicians, 4200 Pine St., Philadelphia 4.

MASSACHUSETTS

Appoint Acting Department Heads.—The appointments of Eric G. Ball, Ph.D., as acting head of the department of biological chemistry and of Dr. Maurice M. Tolman as acting head of the department of dermatology were announced by Dr. George P. Berry, dean of the faculty of medicine, Harvard University, Boston. Dr. Ball, who has served as a member of the faculty of medicine at Harvard since 1940, succeeds Dr. A. Baird Hastings, who has retired and has become a member of the resident research staff at the Scripps Clinic and Research Foundation, La Jolla, Calif. Dr. Ball is professor of biological chemistry at Harvard and chairman of the division of Medical Sciences. Dr. Tolman, assistant clinical professor of dermatology at Harvard, where he has taught since 1940, succeeds Dr. Chester N. Frazier, who retired in 1958. Dr. Tolman is acting chief of the dermatology service at the Massachusetts General Hospital.

MICHIGAN

Personal.—Dr. Starling D. Steiner has been appointed medical director of General Motors, effective December 1. He succeeds Dr. Max R. Burnell, who retired on Nov. 1. Dr. Steiner, who has been medical director of the Oldsmobile Division of General Motors in Lansing since 1946, is currently serving as treasurer of the Ingham County Medical Society.—Dr. William A. Fellner has been appointed medical director of General Motors central office, Detroit, effective Feb. 1. He replaces Dr. William J. Fulton, who is retiring.

Annual Conference on Nutrition.—The fifth annual Nutrition Conference, sponsored by Wayne State University College of Medicine, will be held on Friday, March 20. Speakers on the general subject "Inorganic Factors in Nutrition" will include George K. Davis, Ph.D., of the University of Florida; Dr. William B. Schwartz, of Tufts Medical School; Dr. Carl V. Moore, of Washington University; and David M. Hegsted, Ph.D., of Harvard University. Members of the American Medical Association are cordially invited. For information write Mr. James M. Orten, Chairman, Publicity Committee, Wayne State University, 1401 Rivard St., Detroit 7.

Society News.—The Michigan Academy of General Practice congress of delegates convened Nov. 11 and the following officers were elected: Dr. Clark W. Royer, Battle Creek, installed as president by Dr. Francis P. Rhoades, Detroit, retiring president; Dr. Howard C. Rees, Grosse Pointe, president-elect; Dr. Earl C. Long, Detroit, secretary; Dr. Lyle W. Korum, Detroit, treasurer; Dr. C. Howard Ross, Ann Arbor, speaker; Dr. Aaron C. Stander, Saginaw, vice-speaker.

MISSISSIPPI

Society News.—The Mississippi Academy of General Practice concluded its 10th annual meeting recently with Dr. A. T. Tatum, Petal, raised to presidency. Newly elected officers are Drs. R. J. Moorehead, Yazoo City, president-elect; Louis F. Rittelmeyer, Jackson, vice-president; and J. R Bane, Jackson, secretary-treasurer.

MISSOURI

Dr. Mason to Give Annual Lecture.—Dr. Michael L. Mason, professor of surgery, Northwestern University School of Medicine, will present the 10th annual Dr. F. G. Thompson Sr. Lecture on Thursday evening, May 21, at the Thompson, Brumm, Knepper Clinic and Hospital, in St. Joseph. The title of the lecture will be "Treatment of Acute Injuries to the Hand."

NEW JERSEY

Annual Heart Seminar.—The New Jersey Heart Association will hold its annual scientific seminar in the Essex House Hotel, 1050 Broad St., Newark, April 1, at 2 p. m. The program is as follows:

Surgical Approach to Coronary Artery Disease, Dr. Claude S. Beck, Cleveland.
Current Views on the Causation of Atherosclerosis, Dr. Russell L. Holman, New Orleans.
Controversial Views in the Management of the Atherosclerotic Patient, Dr. Samuel A. Levine, Boston.
The Recognition of the Atypical Coronary Occlusion, Dr. William Likoff, Philadelphia.

Dr. Norman Reitman is president of the New Jersey Heart Association, and Mr. Howard W. Dayton, 60 Park Place, Newark 2, N. J., is executive director.

NEW YORK

Welsh Guest.—Dr. Arthur G. Watkins, Dean of Clinical and Postgraduate Studies at the Welsh National School of Medicine, Cardiff, England, was

the guest of the pediatrics department at Albany Medical College Feb. 16 and 17. Dr. Watkins, who is also professor of child health at the Welsh School and pediatrician at the United Cardiff Hospitals, served as professor pro tem of pediatrics during his stay. He addressed junior medical students on Monday, and spoke before the entire student body and faculty on Tuesday.

Open Applications for Medical Supervisor.—The New York State Department of Civil Service will accept applications until April 10 from qualified candidates for the position of supervisor of school medical services, State Education Department. No written or oral test will be required. Candidates will be rated on their training and experience in relation to the duties and requirements of the position. At present there is one vacancy in Albany and another is anticipated. Candidates must possess a license issued by New York State to practice medicine or be eligible to enter the examination for such a license and must have two years of satisfactory experience in the practice of medicine, of which one year must have included service as a school physician. The annual salary range for this position, which is open only to legal residents of New York State, is $8,750 to $10,520. A supervisor of school medical services performs field and office work in the supervision and guidance of the health services program in the schools of the state. For applications write to Recruitment Unit, New York State Department of Civil Service, State Campus, Albany 1, N. Y.

New York City

Dr. Brunsting to Give Memorial Lecture.—The department of dermatology and syphilology of New York University Post-Graduate Medical School announced that the second Howard Fox Memorial Lecture will be given by Dr. Louis A. Brunsting Sr., April 21, 8 p. m., in the auditorium of Alumni Hall, 550 First Ave., New York City. The title of his talk will be "Porphyria Cutanea Tarda."

Dr. Wangensteen to Lecture.—The annual Walter L. Niles Memorial Lecture, sponsored by Nu Sigma Nu, Tau Chapter, will be given by Dr. Owen H. Wangensteen, chief of surgery, University of Minnesota, Minneapolis, at 8 p. m., March 18, in the auditorium of the Cornell University Medical College, 1300 York Ave., on "Studies in Peptic Ulcer." A dinner in honor of Dr. Wangensteen will be held before the lecture. The lecture is open to medical students and members of the profession.

Hospital News.—The celebration of the 100th anniversary of the third (NYU) surgical division of Bellevue Hospital Center was a highlight of the New York University College of Medicine Alumni Day ceremonies Feb. 21. Dr. Frank B. Berry, assistant secretary of defense (health and medical) and former director of Bellevue's first surgical division, received the University Bronze Medal and gave the principal address of the day. Additional awards presented were the association's annual distinguished service award to Dr. John H. Mulholland, chairman, department of surgery, and the presidential citation to Dr. Henry M. Scheer, former president of the association.

Memorial Fellowship for Cancer Research.—The New York Cancer Research Institute awarded the first Oliver E. Spencer Memorial Fellowship to New York University College of Medicine. The fellowship, established by friends and relatives of the late Oliver E. Spencer, who died of cancer at the age of 25, will provide a one-year training and research scholarship to a physician specializing in cancer and selected by Dr. Donal Sheehan, dean. The first incumbent is Dr. Erlinda Tobillo Novales, of Manila, The Philippines. Upon receiving her M.D. degree in 1955 from Santa Tomas University, she came to the United States for her residency training at New York City's Gouverneur Hospital and the New York Infirmary, where she is now chief resident in medicine.

Neurological Institute Celebrates Anniversary.—The year 1959 marks the 50th anniversary of the founding of The Neurological Institute of New York, specifically set up as a specialty hospital for the medical and surgical treatment of the nervous system. The institute in 1929 became affiliated with the Presbyterian Hospital of New York as a part of the Columbia–Presbyterian Medical Center. To commemorate the institute's 50th anniversary, a series of special events have been planned by Columbia University and the Presbyterian Hospital, and by various societies in neurology and neurosurgery. On March 10 a joint meeting of the New York Neurological Society and the Section of Neurology and Psychiatry of the Academy of Medicine was held. On April 27-28 the Society of Neurological Surgeons will hold its 50th meeting at the institute. A special anniversary celebration will be held at the Columbia–Presbyterian Medical Center May 15-16. Scientific sessions at which alumni and guests will speak will be held and there will be a commemorative dinner at the Waldorf–Astoria Hotel.

On May 16 a special convocation of Columbia University and the Presbyterian Hospital will be held at the Medical Center.

PENNSYLVANIA

Philadelphia

Personal.—Dr. I. S. Ravdin, vice-president for medical development, University of Pennsylvania, and Dr. John McK. Mitchell, vice-provost of the university and dean of the School of Medicine, were appointed to the Surgeon General's Consultant Group on Medical Education, Dr. Leroy Burney, surgeon general of the U. S. Public Health Service has announced.——Dr. Orville C. King was named director of the division of surgery for Pennsylvania Hospital department for sick and injured, Eighth and Spruce Streets. This announcement coincides with Dr. King's appointment as professor of clinical surgery, University of Pennsylvania School of Medicine.

RHODE ISLAND

Dr. Dailey Appointed State Health Director.—Governor Christopher Del Sesto of Rhode Island announced the appointment of Dr. Jeremiah A. Dailey, of Edgewood, as director, Department of Health, State of Rhode Island. Dr. Dailey retired from the United States Army at Fort George G. Meade, Md., Jan. 31. At the time of his retirement he was commanding officer, 68th Medical Group.

Hospital News.—Dr. Henry N. Harkins, professor of surgery and executive officer, department of surgery, University of Washington School of Medicine, Seattle, and surgeon-in-chief, King County Hospital (Seattle), will serve as surgeon-in-chief pro tempore at the Rhode Island Hospital, Providence, on March 19-21.

TENNESSEE

University News.—Dr. James S. Speed, head of the department of orthopedic surgery, University of Tennessee College of Medicine, Memphis, since 1941, has resigned his administrative duties but will continue as professor in the department. Dr. Speed's position as head of the department will be taken by Dr. Harold B. Boyd, who was advanced from associate professor to professor.

TEXAS

Dr. Wallace Wins Caldwell Award.—Dr. Stuart A. Wallace, chairman, department of pathology, was presented with the George T. Caldwell award, naming him "Pathologist of the Year for the State of Texas" at a meeting of the State Clinical Pathologists in Houston. The presentation was made at a banquet Jan. 24 "in recognition of long and distinguished service to mankind in the field of Pathology in Texas." Dr. Wallace has been associated with Baylor College since it was located in Dallas and became chairman of the department when the Houston move was made. The award, in memory of the late Dr. George T. Caldwell, who was professor of pathology at Baylor College of Medicine in Dallas, was established by Mrs. Caldwell and family about five years ago.

VIRGINIA

Meeting of Physicians in Hot Springs.—The American College of Physicians, Virginia Region, will meet March 21 at the Homestead, Hot Springs. Thirteen papers are scheduled for presentation, including the following which have invited guest authors:

Evaluation and Management of Electrolyte Problems in Heart Failure, Drs. Julian R. Beckwith Sr., Nuzhet O. Atuk, and J. Edwin Wood Jr., Charlottesville.

Pathogenesis of the Anemia in Myxedema, Drs. Jason E. McClellan and Byrd S. Leavell, Charlottesville.

Long-Term Anticoagulant Therapy, Drs. Frank E. Taylor, Charles L. Crockett Jr., and R. Earle Glendy, Roanoke.

The Coagulation Deficiencies with Report of a Case of Christmas Disease, Dr. Harry I. Johnson, Roanoke.

The Co-Existence of Pheochromocytoma and Unilateral Adrenocortical Hyperplasia, Drs. Gerald A. Williams, Charlottesville, William W. S. Butler, III, Roanoke, and Kenneth R. Crispell, New York City.

Clinical Usefulness of a Potent New Oral Diuretic, Drs. Gordon F. Cavell, Eugene M. Wyso, and David W. Richardson, Richmond.

Cardiotoxic Effects of Quinidine and Its Treatment with Molar Sodium Lactate, Dr. Dewey J. Bailey, Charlottesville.

A business meeting will precede a meeting with the Virginia Society of Internal Medicine at 4 p. m. Guest speaker will be Dr. Dwight L. Wilbur, San Francisco, president of the college. Dr. Charles M. Caravati is governor of the college for Virginia.

WEST VIRGINIA

Surgeons Meeting in White Sulphur Springs.—The annual meeting of the West Virginia Chapter of the American College of Surgeons will be held at The Greenbrier in White Sulphur Springs, April 3-4. Dr. Cornelius E. Sedgwick, of the Lahey Clinic, will present papers on "Portal Hypertension," "Tumor of the Neck," and "Surgical Treatment of

Thyroid Disease." Dr. David M. Hume, chairman, department of surgery, Medical College of Virginia, Richmond, will speak on a surgical subject of general interest. A cordial invitation has been extended by the West Virginia Chapter to all practicing physicians in the state. Information may be obtained by writing Dr. Victor S. Skaff, Secretary, West Virginia Chapter, ACS, 807 Atlas Building, Charleston 1, W. Va.

Appoint Acting Director of Mental Health.—Dr. Margaret T. Ross, director of community service, West Virginia State Department of Mental Health, was named by Governor Cecil H. Underwood as acting state director of mental health. She succeeds Dr. William B. Rossman of Charleston, who resigned. Dr. Richard J. Lilly, of Weston, superintendent of Weston State Hospital, had been appointed as successor to Dr. Rossman, and he came to Charleston and took the oath of office. However, late in January the question of Dr. Lilly's eligibility for the office was raised, inasmuch as he has not been a citizen of West Virginia for one year, as required by state law. On Feb. 4, the appointment of Dr. Lilly was withdrawn temporarily by Governor Underwood, who at that time indicated that he will reappoint him to the office next May, when he will have been a resident of the state for a year.

WISCONSIN

Dr. Morton Wins Award.—Newton E. Morton, Ph.D., assistant professor of medical genetics in the University of Wisconsin Medical School, Madison, was named to receive the Lederle Medical Faculty award of $18,000, given by the Lederle Laboratories and designed "to provide support for continued development of a promising teacher and investigator in fields of medicine and human biology." Dr. Morton, who serves as an associate editor of the *American Journal of Human Genetics*, will be supported under the grant for three years.

GENERAL

Booklet on Manuscript Preparation.—To facilitate the work of authors and editors of their journals, S. Karger, Inc., recently issued a booklet containing some rules for the preparation of manuscripts and bibliographies with a list of abbreviations of titles of current medical periodicals. The abbreviations of titles of periodicals have been taken with some minor deviations, from the list of World Medical Periodicals compiled by the World Medical Association based on the World List of Scientific Periodicals prepared under the auspices of UNESCO. The booklet has also been issued in German and French. For information write S. Karger, Inc., Swiss Bank Corporation, New York City.

Citizens' Committee on Health.—Formation of an ad hoc citizens' committee to increase public understanding of the principles underlying increased United States support of international health work was announced Feb. 12 by Dr. Howard A. Rusk in an address before a Brotherhood Week Luncheon of the National Conference of Christians and Jews in New York City. General Omar Bradley is chairman of the new group, known as the Committee on Health for Peace, and Detlev W. Bronk, LL.D., president, Rockefeller Institute for Medical Research, is chairman of its Scientific Advisory Committee. The Committee on Health for Peace will not engage in fund-raising activities; nor will it attempt to duplicate the work of the National Citizens Committee for the World Health Organization. Its function will be solely to increase public understanding of the importance of international cooperation in health and medical research. The activities would be entirely educational and would be initially centered on the International Health and Medical Research Act of 1959 which has been introduced in the Senate by Senator Lister Hill, Alabama, with 58 senators as co-sponsors, and in the House of Representatives by Representative John Fogarty, Rhode Island.

Invite Nominations for Research Award.—Nominations for the eighth Kimble Methodology Research Award are being accepted until June 1, 1959. This award, which gives recognition to the application of scientific knowledge to the Public Health Laboratory, was established by the Kimble Glass Company of Toledo, Ohio (subsidiary of the Owens–Illinois Glass Company), and is sponsored by the Conference of State and Provincial Public Health Laboratory Directors. The award of $1,000 and silver plaque will be presented at the annual meeting of the conference to be held in Atlantic City, N. J., in October. Rules governing nominations include:

(1) The candidate's work should be either:
   a. A fundamental contribution which serves as a baseline for development of diagnostic methods which fall within the province of the public health laboratory.
   b. The adaptation of a fundamental contribution to make it of use in a diagnostic laboratory.

(2) Candidates should be from the United States, its territories, or Canada.

(3) Nominations must be covered by six reprints with six summaries and bibliography or, if reprints are not avail-

able, by six summaries with bibliography. A statement which justifies the recommendations of the study must be included.

(4) Nominations may be made by the authors, associates, or by others. Documentary evidence, etc., should not be signed by the nominator. The nomination, however, should be accompanied by a letter of transmittal.

(5) Nominations received after June 1 will be considered for nomination in 1960.

(6) Nominations of a piece of work where there is more than one author is permissible. (If such work is selected, division of the cash award shall be arranged between the workers themselves.)

(7) The materials submitted to the Nominating Committee will not be returned to the sender.

Send nominations to E. T. Bynoe, Ph.D., Chairman, Nominating Committee, Kimble Award, Laboratory of Hygiene, Department of National Health and Welfare, Ottawa, Ontario, Canada.

CANADA

Prize for Paper on Fertility.—The Canadian Society for the Study of Fertility announced the award of the 1958 "Ortho" prize to Dr. Charles P. Leblond and Assistant Professor Y. Clermont, of the department of anatomy, McGill University, for their paper on "Differentiation and Renewal of Spermatagonia in the Monkey Macacus Rhesus." The "Ortho" prize was $1,000 for 1958, as the prize of $500 for 1957 was not awarded and had accumulated. Those interested in submitting a paper to the society for the 1959 "Ortho" prize of $500 must do so before June 1. Details may be obtained through Dr. Jean F. Campbell, Secretary-Treasurer, The Canadian Society for the Study of Fertility, 238 Queen's Ave., London, Ontario.

FOREIGN

Pediatric Convention in Italy.—Under the auspices of the Italian Society for Pediatrics (Societa Italiana di Pediatria) an International Pediatric Convention of the Latin Nations, will be held in San Remo, Italy, Sept. 24-27. The convention will be under the chairmanship of Prof. Giovanni De Toni, director of the pediatric clinic "Gaslini" of the University of Genova. The topics for discussion will be the following:

(1) Regional Pathology—the speakers chosen will report on the infantile pathology predominant in their respective regions, and on its changes during the last 20 years.

(2) Disease of Metabolism—the speakers will report on the specific topic of research.

(3) The Growth of the Child, Normal and Pathological Conditions.

Papers on the three topics will be accepted. For any information write to the Secretaries of the Convention (Dott. Prof. Ettore De Toni e Dott. Prof. Piero Salomone) c/o Pediatric Clinic "Gaslini," Genova-Quarto, or to the President of the Executive Committee: Dott. Prof. Giuseppe Cotellessa c/o Azienda Autonoma di Soggiorno e Turismo, Palazzo Riviera, San Remo (Italy).

Congress of Red Cross in Spain.—Dr. Carlos Blanco Soler, president of the first National Medical Congress of the Red Cross of Spain, has announced that the congress will be held in Madrid, May 20-23, under the auspices of the Higher Assembly of the Red Cross. Official topics are as follows:

Radioactivity.
Congenital Heart Diseases: Clinical, Diagnosis and Treatment of Interauricular Defects.
Rehabilitation and Recuperation of Invalids.
Blood Transfusion.

There will be a symposium on medicine and surgery of emergency, with Dr. Soler presiding. For information and registration write the Secretaria General Asamble Suprema, Paseo de Eduardo Dato, 16, Madrid, Spain.

Congress of Health Workers in Paris.—The sixth International Health Workers' Congress and Equipment Exhibition will be held in Paris, at the Parc des Expositions (Porte de Versailles), June 9-12 under the auspices of the journal "Techniques Hospitalieres Medico-Sociales et Sanitaires." It will be organized under the patronage of the French Minister of Public Health and the Population. The central theme will be "The Patient in the Hospital of the Future—The Functions of the Health Team." The chairman of the congress is Dr. Le Gorgeu, member of the Council of State and chairman of the National Committee for Hospital Organization. Hospital workers from all countries are cordially invited to participate. A hospital exhibition will include models of operating suites, wards, laboratories and technical equipment. Information on the program, exhibition space, hotel accommodation, etc., may be obtained from the Secretary-General, 37 rue de Montholon, Paris 9e.

DEATHS IN OTHER COUNTRIES

Dr. Gerin-Lajoie Dies.—The president-elect of the World Medical Association, Dr. Leon Gerin-Lajoie, Canadian gynecologist, died Feb. 14. He was president of the International Federation of Obstetricians and Gynecologists and vice-dean of the faculty of medicine at the University of Montreal. Dr.

Gerin-Lajoie was a founder of the Quebec division of the Canadian Medical Association and had served as its president.

CORRECTION

Report on 1958 Mortality.—In an item appearing in the Feb. 14 issue of THE JOURNAL, Medical News section, under this side head, the figures 916 per 1,000 and 912 should have read 9.6 and 9.2, respectively.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Phoenix, April 5-10. Applications now on file. *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Boston, April 16-19. Final date for filing application was Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PHYSICAL MEDICINE AND REHABILITATION: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Public Health.* Minneapolis, Boston, Baltimore, Chapel Hill, North Carolina and New Orleans, April 9-11; Berkeley, Calif., April 23-25; Pittsburgh, April 16-18. *Occupational Medicine.* Chicago, April 24-26. *Aviation Medicine.* Los Angeles, April 24-26. Final date for filing all applications is March 16. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: *Oral.* Los Angeles, September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

AMERICAN BOARD OF UROLOGY: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

NAVY

Tissue Bank Training Course.—A two-week Tissue Bank Training Course offered at the National Naval Medical Center, Bethesda, Md. is now available to any eligible inactive naval reserve medical officer. This training may commence on any Monday morning and provides orientation in the operation and administration of a tissue bank. It includes (1) indoctrination in the methods of tissue procurement; (2) storage and dispensing; (3) tissue culture; (4) tissue chemistry; (5) processing excised tissue and allied short and long-term research projects in the tissue culture and tissue chemistry fields; (6) indoctrination in the medicolegal aspects of homotransplantation; (7) the procedure for obtaining permission for tissue donations; and (8) familiarization with the operation of the Tissue Bank Registry and all other administrative practices associated with tissue banking.

Reserve medical officers from the First, Third, Fourth, Fifth, Sixth, Eighth, and Ninth Naval Districts may attend this course on a limited quota basis authorized by the chief of naval personnel. Security clearance is not required.

Surgeon General Reappointed.—Rear Adm. Bartholomew W. Hogan was reappointed as surgeon general of the Navy for a period of two years, or until Feb. 15, 1961. He entered the service on June 6, 1925. In the early months of World War II, he served on the USS Wasp and was aboard that carrier when she was torpedoed in the South Pacific on Sept. 15, 1942. For heroic service during this action, he was awarded the Silver Star medal.

Personal.—Capt. A. J. Cerny has assumed command of the U. S. Naval Hospital, Guantanamo Bay, Cuba, relieving Capt. L. A. Newton, who retired on Jan. 31. Other medical officers retired were Captains F. V. Berley, M. J. Hantover (temporary disability), G. A. Gray, and H. L. Weaver.

VETERANS ADMINISTRATION

Treatment Centers for Mental Illness.—The first mental hygiene day center for treatment of veterans with service-connected mental illness was established at the VA outpatient clinic in Brooklyn, N. Y. More such clinics will be established within the next few years. The day center program is designed primarily to provide more and better outpatient treatment for the increasing number of veterans being released from VA hospitals after treatment for service-connected schizophrenia. Many of these patients need a great deal of help through the VA outpatient treatment program if they are to adjust to community living and avoid rehospitalization. The clinic director, Dr. Philip R. Casesa, said about 75 patients will spend the major part of their time at the new day center in a therapy and planned living program under the supervision of psychiatrists, psychologists, and social workers. In addition to individual and group psychotherapy and educational and occupational therapy, this program will include social and recreational activities carried out with the assistance of volunteers from the community. New tranquilizing drugs and improved treatment programs are increasing the number of patients, especially schizophrenics, being released from VA mental hospitals.

PUBLIC HEALTH SERVICE

Health Statistics.—A new report entitled "Hospitalization—Patients Discharged from Short-Stay Hospitals, July 1957-June 1958" has been published by the Public Health Service. For this report, the surveyed population consisted of the civilian noninstitutional population of the country. The data refer to persons in this population group who were discharged from the hospitals during the year. The short-stay hospitals include general, maternity, and other types in which most patients stay for less than 30 days. The number of patients discharged from such hospitals averaged 99.4 per 1,000 of the surveyed population. Among the group discharged, the average length of stay was 8.6 days. Next to childbirth, the most frequent cause of hospitalization was the respiratory diseases, including tonsil and adenoid conditions. The report is Public Health Service Publication no. 584-B7 and may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 30 cents per copy.

Clinical Center Pamphlet Series.—The Clinical Center at the National Institutes of Health is publishing a series of pamphlets describing the methods and procedures used at the center. The first, "A Manual for Metabolic Balance Studies" by Marie M. Ceglarek, R.N., Bertha E. Bryant, R.N., and G. Donald Whedon, M.D. (PHS publication no. 607), is now available at 20 cents a copy from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

Personal.—Dr. William B. Sherman, associate attending physician of Presbyterian Hospital and attending physician at Roosevelt Hospital, New York City, and Dr. William W. Frye, professor of tropical medicine and dean of the school of medicine, Louisiana State University, New Orleans, have been appointed to the National Advisory Allergy and Infectious Diseases Council. They will advise and make recommendations to the surgeon general regarding research grants.

DEATHS

Anderson, Donald Carl Ⓜ West Palm Beach, Fla.; University of Minnesota Medical School, Minneapolis, 1945; interned at the Naval Hospital in San Diego, Calif.; veteran of World War II and Korean War; died Dec. 8, aged 41.

Ard, Robert Wilson Ⓜ Hagerstown, Md.; Syracuse University College of Medicine, 1948; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; resigned from the regular Navy on March 6, 1953; served in the U. S. Public Health Service Reserve; veteran of World War II and Korean War; died Dec. 20, aged 34.

Arneberg, John Gyro, Grand Forks, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; associated with Grand Forks Deaconess Hospital and St. Michael's Hospital; died Dec. 17, aged 83.

Audet, Louis Eugene Ⓜ Williamsport, Pa.; Tufts College Medical School, Boston, 1930; died in the Divine Providence Hospital Dec. 19, aged 54.

Bachman, David Floyd Ⓜ Bethlehem, Pa.; Medico-Chirurgical College of Philadelphia, 1912; formerly county coroner; died in St. Luke's Hospital Dec. 22, aged 74.

Barrow, John Vincent Ⓜ Los Angeles; Rush Medical College, Chicago, 1911; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served on the faculties of the College of Medical Evangelists in Loma Linda and Los Angeles and the Medical Department of the University of Southern California; past-president and vice-president of the Los Angeles County Medical Association, of which he was a councilor; served on the staffs of the California, Los Angeles County, and St. Vincent's hospitals, and the Hospital of the Good Samaritan; died Dec. 17, aged 81.

Batory, Roman Julius Ⓜ Stroudsburg, Pa.; Hahnemann Medical College of Philadelphia, 1930; interned at Women's Homeopathic Hospital in Philadelphia, where he served a residency; served a residency at Hamburg State Sanatorium for Tuberculosis in Hamburg; veteran of World War II; member of the American College of Chest Physicians; on the staff of the General Hospital of Monroe County in East Stroudsburg; died Dec. 21, aged 55.

Ⓜ Indicates Member of the American Medical Association.

Blumenschein, John Charles Ⓜ Independence, Mo.; Washington University School of Medicine, St. Louis, 1943; interned at Virginia Mason Hospital in Seattle; served a residency at St. Joseph Infirmary in Atlanta, Ga.; associated with the Independence Sanitarium and Hospital; died in Mogate, Honduras, Central America, Dec. 14, aged 40.

Blydenburgh, George Dean, Byesville, Ohio; University of Cincinnati College of Medicine, 1946; interned at White Cross Hospital in Columbus, Ohio; formerly an officer in the medical corps, Army of the United States; died in Columbus Dec. 28, aged 37.

Booth, George Randolph Ⓜ Wilburton, Okla.; Memphis (Tenn.) Hospital Medical College, 1904; died in the McAlester (Okla.) Hospital Dec. 14, aged 74.

Bowles, James Puryear Ⓜ Captain, U. S. Navy, retired, Richmond, Va.; Medical College of Virginia, Richmond, 1911; entered the U. S. Navy Jan. 24, 1921, and retired March 1, 1947; died in the U. S. Naval Hospital Philadelphia, Dec. 24, aged 73.

Breckwedel, Harry Benjamin, Newport Beach, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1900; died Dec. 18, aged 85.

Cannon, Vern Edward, Decatur, Ill.; Chicago College of Medicine and Surgery, 1914; veteran of World War I; on the staff of St. Mary's Hospital; died Jan. 6, aged 68.

Catto, William Bruce Ⓜ El Reno, Okla.; University of Louisville (Ky.) Medical Department, 1908; on the staff of the Park View Hospital; died in Oklahoma City Dec. 7, aged 75.

Cloutier, Doria Marie, Albuquerque, N. M.; University of Wisconsin Medical School, Madison, 1950; died in the Bernalillo County–Indian Hospital Dec. 17, aged 36.

Cochran, J. Lawrence Ⓜ Carroll, Iowa; University of Tennessee College of Medicine, Memphis, 1931; veteran of World War II; president of the Carroll County Medical Society; county coroner; secretary-treasurer of the Iowa Coroners Association; member of the Aero Medical Association; associated with St. Anthony's Hospital, where he died Dec. 24, aged 50.

Coulter, William James, Toledo, Ohio; Toledo Medical College, 1900; served as a member of the staff of the Toledo Hospital; died Dec. 10, aged 91.

Crounse, Kenneth Eugene Ⓜ Albany, N. Y.; Albany Medical College, 1924; veteran of World War I; formerly on the faculty of his alma mater; consultant, Moses–Ludington Hospital in Ticonderoga; died in Delray Beach, Fla., Dec. 26, aged 61.

Darrin, Charles Bennett, Seattle; Bellevue Hospital Medical College, New York City, 1887; died in the King County Hospital, Harborview Dec. 3, aged 94.

Decker, Elmer Raymond Ⓜ Sunbury, Pa.; Medico–Chirurgical College of Philadelphia, 1910; veteran of World War I; consultant at Federal Penitentiary at Lewisburg; on the staff of the Evangelical Community Hospital in Lewisburg, where he died Dec. 27, aged 73.

Dreibrodt, Ben Allen Ⓜ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1938; veteran of World War II; on the staffs of St. Benedict's, Santa Rosa, and Baptist Memorial hospitals; died in the Robert B. Green Hospital Dec. 22, aged 45.

Fialk, Harry Ⓜ Union City, N. J.; Tulane University School of Medicine, New Orleans, 1929; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the North Hudson Hospital in Weehawken, and the Medical Arts Center Hospital in New York City, where he died Dec. 27, aged 54.

Godfrey, Lincoln Jr. Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1942; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; research director of the National Council on Alcoholism; veteran of World War II; served on the faculty of his alma mater; on the staff of the Presbyterian Hospital; died Dec. 18, aged 43.

Green, Hyman Ⓜ Boston; Harvard Medical School, Boston, 1914; joined the British Expeditionary Forces in World War I and transferred later, as a captain, to the U. S. Army; member of the American Academy of Pediatrics; past-president of the Greater Boston Medical Association, New England Pediatric Society, and the Children's Hospital Alumni Association; associated with Children's and Beth Israel hospitals; died in the Veterans Administration Hospital Dec. 27, aged 68.

Grimes, Ivison, Camden, Texas; University of Tennessee College of Medicine, Memphis, 1914; died Dec. 11, aged 67.

Haight, Vincent Wymand Ⓜ Buchanan, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1919; veteran of World War I; an examining physician for the Metropolitan Life Insurance Company; since 1923 school physician of Central School District No. 3, town of Cortlandt; served as health officer for the village of Buchanan; on the staff of the Peekskill (N. Y.) Hospital; died in the Memorial Hospital, New York City, Dec. 7, aged 63.

Healey, Edward Joseph Gerard Ⓜ Weston, Mass.; Tufts College Medical School, Boston, 1943; veteran of World War II; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology, Inc.; member of the American College of Radiology; radiologist at Waltham (Mass.) Hospital; associate radiologist at the Boston City Hospital; died in St. Elizabeth's Hospital, Boston, Dec. 13, aged 39.

Moet, Joe Louis Ⓜ La Feria, Texas; Baylor University College of Medicine, Dallas, 1941; veteran of World War II; a past-president of the Cameron–Willacy Counties Medical Society; member of the American Academy of General Practice; a member of the school board for the La Feria Independent School District; at one time chief of staff of Valley Baptist Hospital at Harlingen; died Oct. 20, aged 42.

Moore, Neil S. Ⓜ St. Louis; St. Louis University School of Medicine, 1913; on the faculty of his alma mater; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; past-president of St. Louis Medical Society; on the staffs of St. Louis County Hospital in Clayton, St. Anthony's Hospital, and Alexian Brothers Hospital; died Dec. 5, aged 71.

Moreland, James Thaddeus, Idabel, Okla.; Chattanooga (Tenn.) Medical College, 1901; veteran of World War I; died Nov. 22, aged 87.

Nauss, Ralph Welty, Gainesville, Fla.; Northwestern University Medical School, Chicago, 1905; formerly on the faculty of Cornell University Medical College in New York City, where he was on the staff of the New York Hospital; spent three years in the medical mission field in Belgian Congo; author of "Medical Parasitology and Zoology"; died in the University of Florida Infirmary Dec. 15, aged 82.

Northrup, John Fredrick Ⓜ Topeka, Kan.; College of Homeopathic Medicine and Surgery of the Kansas City University, Kansas City, Mo., 1899; died in the Stormont–Vail Hospital, Dec. 7, aged 83.

Owen, Harbert Claude Ⓜ Holly Bluff, Miss.; Memphis (Tenn.) Hospital Medical College, 1902; died in the King's Daughters' Hospital, Yazoo City, Dec. 21, aged 80.

Plaut, Clarence Theodore Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1926; on the staff of the Jackson Park Hospital, where he died Jan. 5, aged 57.

Pontius, Guy Victor Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1923; associate professor of surgery at Northwestern University Medical School; on the staffs of the St. Francis Hospital in Blue Island, St. Luke's Hospital, and Illinois Central Hospital; died Jan. 4, aged 61.

Price, Oscar Jay Ⓜ Somerville, Mass.; Tufts College Medical School, Boston, 1901; for 40 years medical examiner for Metropolitan Life and Prudential Insurance companies; died in the Somerville Hospital Dec. 9, aged 84.

Rife, Dwight William Ⓜ Farmington, N. M.; University of Illinois College of Medicine, Chicago, 1931; interned at the Lutheran Deaconess Home and Hospital in Chicago; veteran of World War I; commander in the U. S. Naval Reserve during World War II and was in the invasion of Okinawa, receiving the Bronze Star as a result of his performance at that time; died Dec. 21, aged 62.

Rock, Thomas Stephen Ⓜ Lancaster, N. H.; Columbia University College of Physicians and Surgeons, New York City, 1947; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; member of the staff and chief of surgery at Beatrice Weeks Memorial Hospital; formerly associated with the Veterans Administration Hospital, White River Junction, Vt.; died in the Mary Hitchcock Hospital, Hanover, Nov. 27, aged 36.

Sachs, Ernest Ⓜ North Haven, Conn.; born in New York City Jan. 25, 1879; Johns Hopkins University School of Medicine, Baltimore, 1904; on the faculty of Yale University School of Medicine in New Haven; professor emeritus of neurological surgery at Washington University School of Medicine in St. Louis, where he was on the staffs of the Ellis Fischel State Cancer Hospital in Columbia, Barnes, St. Louis Children's, St. Louis Maternity, and St. Louis City hospitals; past-president of the American Neurological Association; past-president and secretary of the Society of Neurological Surgeons; member of the Southern Surgical Association, American Physiological Association, St. Louis Surgical Society, Sigma Xi, and Phi Beta Pi; fellow of the American College of Surgeons and the International College of Surgeons; member of the founders group of the American Board of Surgery; specialist certified by the American Board of Neurological Surgery; author of many books; died in the Grace–New Haven Memorial Hospital in New Haven Dec. 2, aged 79.

Schloss, Max Ⓜ Jackson Heights, N. Y.; Ludwig–Maximilians–Universität Medizinische Fakultät, Munchen, Bavaria, Germany, 1924; member of the American Society of Anesthesiologists; died in New York City Nov. 20, aged 60.

Schussler, Edward G. Ⓜ Oaklawn, Ill.; Chicago College of Medicine and Surgery, 1908; associated with Little Company of Mary Hospital in Evergreen Park and the South Chicago Community Hospital in Chicago; died in Chicago Dec. 16, aged 72.

Scibetta, Louis Joseph, Erie, Pa.; Detroit College of Medicine and Surgery, 1928; an associate member of the American Medical Association; died in St. Vincent's Hospital Dec. 17, aged 58.

Segal, Marek M. Ⓜ New York City; Uniwersytet Jozefa Pilsudskiégo, Warszawa, Poland, 1924; associated with the Hospital for Joint Diseases; died in Lake Mahopac, N. Y., Dec. 7, aged 60.

Shoun, Alexander Nelson Ⓜ San Manuel, Ariz.; Jefferson Medical College of Philadelphia, 1932; member of the American Rheumatism Association; president of the Pinal County Medical Society; formerly practiced in Winston–Salem, N. C., where he was school physician with the city department of health; associated with the San Manuel Cooper Corporation Hospital; died Dec. 12, aged 51.

Smith, Clarence B., Roff, Okla.; University of Texas School of Medicine, Galveston, 1899; died in the Valley View Hospital in Ada Dec. 2, aged 82.

Smith, Edward Greer Ⓜ Mercedes, Texas; Dallas Medical College, 1904; for 32 years served the Missouri–Pacific Railroad as local physician; died Dec. 10, aged 86.

Stanka, Andrew George Ⓜ Grand Ledge, Mich.; University of Michigan Department of Medicine and Surgery, Minneapolis, 1909; member of the American Academy of General Practice; served on the staff of the St. Lawrence Hospital in Lansing; died Dec. 13, aged 79.

Strecker, Edward Adam, Philadelphia; born in Philadelphia Oct. 16, 1886; Jefferson Medical College of Philadelphia, 1911; named professor of nervous and mental diseases at his alma mater in 1925, serving until 1931, and in that year became professor and head of the department of psychiatry at the University of Pennsylvania School of Medicine, where he remained in that capacity until he became professor emeritus in 1953; emeritus professor of psychiatry at the University of Pennsylvania Graduate School of Medicine; clinical professor of psychiatry and mental diseases at Yale University in New Haven, Conn., from 1926 to 1932; appointed as the first professor of psychiatry at the Seton Hall College of Medicine and Dentistry, Jersey City; in 1939 was selected to deliver the Salmon Lectures on psychiatry and mental hygiene; gave the Pasteur, Menas Gregory Memorial, and Bernard McGhie Memorial lectures in 1946; specialist certified by the American Board of

Psychiatry and Neurology; an associate member of the American Medical Association; member and past-president of the American Psychiatric Association; member and formerly vice-president of the American Neurological Association; member of the American Psychosomatic Society, the Association for Research in Nervous and Mental Diseases, Alpha Omega Alpha, Sigma Phi Epsilon, and Alpha Kappa Kappa; fellow of the American College of Physicians; on May 24, 1944, received the Dr. I. P. Strittmatter Award of the Philadelphia County Medical Society "in recognition of his distinguished service in the field of psychiatry and mental hygiene and his unselfish devotion to the highest ideals of the profession as physician, teacher, author and consultant in civilian and military medicine"; during World War I held the rank of major in the medical corps of the U. S. Army, as division neuropsychiatrist for the 28th division in France; during World War II named special consultant to the Secretary of War for the Air Forces of the U. S. Army; on Jan. 16, 1948, was awarded the Presidential Certificate of Merit in recognition of his services as consultant to the Surgeon General of the Navy since May 6, 1943; the new building at the New Jersey Neuro-Psychiatric Institute, Princeton, dedicated in 1957 was named after him; since 1917 medical and clinical director of the Pennsylvania Hospital Department for Mental and Nervous Diseases; served as chief of service and consultant at the Institute for Mental Hygiene at Pennsylvania Hospital, consultant to the U. S. Public Health Service, to Bryn Mawr College, and to the U. S. Veterans Bureau; author of more than 200 published papers and several books on psychiatry; died in the Jefferson Medical College Hospital Jan. 2, aged 72.

Tanner, Kirby, Covington, Ky.; Medical College of Ohio, Cincinnati, 1900; died in the Kenton County Infirmary Nov. 8, aged 85.

Thiery, Raymond Donle Ⓜ South Bridgewater, Mass.; Harvard Medical School, Boston, 1923; died in St. Luke's Hospital, Middleboro, Nov. 26, aged 62.

Thompson, Clara Mabel, New York City; Johns Hopkins University School of Medicine, Baltimore, 1920; member of the Medical Society of the State of New York, American Psychoanalytic Association, American Psychosomatic Society, American Psychiatric Association, and the American Psychopathological Association; served as vice-president of the Association for the Advancement of Psychoanalysis; formerly on the faculty of the New York Medical College, Flower and Fifth Avenue Hospitals, and her alma mater; executive director of the William Alanson White Institute of Psychiatry, Psychoanalysis and Psychology; died Dec. 20, aged 65.

Turner, Oliver William Ⓜ Boothbay Harbor, Maine; Jefferson Medical College of Philadelphia, 1893; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; formerly on the staffs of the Augusta General and Augusta State hospitals in Augusta; died in Jackson Heights, N. Y., Nov. 24, aged 90.

Van Horne, Thomas Calvin, Pittsburgh; Medical Department of the Western University of Pennsylvania, Pittsburgh, 1903; an associate member of the American Medical Association; died Dec. 7, aged 83.

Van Tromp, Homer Ovid, Buckhannon, W. Va.; Eclectic Medical College, Omaha, 1913; an associate member of the American Medical Association; past-president and secretary of the Central West Virginia Medical Society; formerly assistant superintendent and clinical director of Weston (W. Va.) State Hospital, where for one year he was acting superintendent; died Dec. 16, aged 81.

Walch, Joseph Francis Ⓜ Lawrence, Mass.; Tufts College Medical School, Boston, 1904; charter member and medical director of the Lawrence Tuberculosis Association; in 1956 awarded a plaque by the Greater Lawrence Tuberculosis Association for his services as medical advisor since 1912; on the staffs of the Clover Hill Hospital, Lawrence General Hospital, and McGowan Memorial Hospital; died Dec. 5, aged 85.

Wapstra, Ilse Sigrid Ⓜ New York City; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1931; died Dec. 29, aged 53.

Ward, William Trulock Ⓜ Salt Lake City; Columbia University College of Physicians and Surgeons, New York City, 1908; for many years on the staff of the Holy Cross Hospital; a member of the board of directors of the First Federal Savings and Loan Association; died Dec. 10, aged 78.

Williams, William Lee, Florence, S. C.; Meharry Medical College, Nashville, Tenn., 1915; died Oct. 1, aged 57.

Willis, James Clinton Jr. Ⓜ Shreveport, La.; Tulane University School of Medicine, New Orleans, 1916; fellow of the American College of Surgeons; president of the Willis–Knighton Memorial Hospital; chairman of the board of directors of Louisiana Bank and Trust Company; senior surgeon for the Illinois Central Railroad; died Dec. 14, aged 67.

Wingquist, Carl Gustave, Crosby, Minn.; University of Minnesota Medical School, Minneapolis, 1932; veteran of World War II; on the staff of the Miners' Hospital, where he died Nov. 4, aged 53.

Wright, Oren Henry Ⓜ Chicago; Rush Medical College, Chicago, 1912; died Dec. 30, aged 73.

FOREIGN LETTERS

AUSTRIA

Operations on the Mentally Ill.—At the meeting of the Society of Physicians in Vienna on Jan. 9, Drs. E. Ringel and H. Schinko stated that a physician is authorized to operate on a patient without the patient's consent if the patient's life is in danger, as in rupture of the stomach. Should the physician establish the diagnosis of a cancer, the operation would also be considered "vitally indicated" inasmuch as the life of the patient is threatened if he is not operated on, but in this case consent of the patient is absolutely necessary. This consent may not be given, however, by a patient with organic dementia, involutional melancholia, amentia, and some types of severe neurosis. Sufficient improvement of the mental disorders, with the exception of some forms of dementia, can be expected today with suitable therapy so that the patient may consent to operation. This year nine patients who had not consented to operation did so after they had been treated at the university neuropsychiatric clinic. These patients are in a good physical and mental condition today. This solution is preferred to operation without the consent of the patient even when he is mentally ill. As to patients with neurosis, the speakers emphasized that their tendency to self-injury may manifest itself in a rejection of an operation or by urging the surgeon to perform an unnecessary operation. In the first instance the psychiatrist should try to persuade the patient to see the surgeon, and in the second instance the surgeon should send the patient to the psychiatrist.

Shorter Hours Requested for Physicians.—The Federal Branch Group of Hospital Physicians have requested shorter hours similar to those already approved for many other professional groups. In letters which were mailed to various hospital managers, attention was called to the enormous work load which has been placed on the hospital physicians and the following demands were listed: (1) a 45-hour week for those hospital physicians who perform their services according to service-agreements with a fixed time of service (up to now, a 48-hour week) in accident-hospitals and in institutions of the District Sick Insurance Funds, (2) every other Saturday off duty, and (3) in hospitals in which, for medical or administrative reasons, a free Saturday every second week cannot be granted, a 10% increase in basic salary.

The items in these letters are contributed by regular correspondents in the various foreign countries.

CANADA

Paralysis Agitans.—DeJong (*Canad. Serv. M. J.* 14:695, 1958) called attention to the difficulty of defining paralysis agitans. Neither the anatomic definition as a disease of the substantia nigra nor the physiological definition as a disorder of the extrapyramidal system is satisfactory. The average physician probably diagnoses the condition on evidence of muscle rigidity and tremor of the limbs, which means that some patients with pulmonary complications due to rigidity of the chest wall or others with neurogenic bladder may not be recorded correctly, and absence of classic features may further diminish the recorded incidence. Canadian Sickness Survey figures suggest a general morbidity for the population of 0.30 per 1,000, rising to 0.85 for the age group from 45 to 64 and 1.52 for those over 65 years of age. DeJong believes that the incidence quoted for the United States of 1,000,000 to 1,500,000 cases is way out of line with Canadian figures. The death rate in Canada for this disease from 1931 to 1956 ranged widely, from 1.42 to 2.49 per 1,000—probably a reflection of the difficulty of accurate diagnosis and recording.

Unlawful Practice Charge.—A charge brought in Ontario of unlawful practice of medicine received a great deal of unfortunate publicity in the press, and the situation was not entirely clarified until the recent publication of an official letter from the provincial College of Physicians and Surgeons in the *Ontario Medical Review*. An English physician was engaged by the Canadian Department of Indian Affairs to treat Indians on an Ontario reservation. For this purpose it was not required that he be licensed in the province (a step which would have involved an internship and examination), provided he treated only Indians of the reservation. Information received by the provincial licensing body indicated that the physician was attending private patients, in spite of a warning to desist, and charging fees. An inspector from the licensing body visited the doctor alleging certain symptoms, received treatment, and was charged $5 for which he was given a receipt on an official government form. A charge was then laid by the inspector of "professing to practice medicine while unregistered under the Ontario Medical Act."

When the case came to court, the Department of Indian Affairs provided defense counsel and one of their officials gave evidence that there was an

agreement with local physicians, who were overworked, that the government physician could see patients in an emergency and hand over his fees to the government, which this physician had scrupulously done. The magistrate dismissed the charge. In the official statement from the licensing body, the letter indicated that it would not appeal the decision, on the grounds that the case is not of sufficient importance and that its proper function is to place evidence before a court rather than to strive for conviction of the person charged.

Thermal Responses to Drugs.—Medical literature contains confusing reports of the effects of some drugs on body temperature. For instance, it has been suggested that ergot may cause hypothermia, hyperthermia, or no change in body temperature. Shemano and Nickerson (*Canad. J. Biochem. & Physiol.* **36**:1243, 1958) have clarified this situation with some experiments on rats given drugs at various ambient temperatures. The drugs investigated included chlorpromazine, ergotamine, Hydergine, *d*-lysergic acid diethylamide (LSD 25), serotonin, and reserpine. They were injected subcutaneously with subsequent hourly recording of the colonic temperature. The room temperature was varied and it was shown that chlorpromazine produced hypothermia at ambient temperatures of 30 to 33 C, no significant effect at 36 C, and hyperthermia at 39 C. Similarly, Hydergine, ergotamine, serotonin, and LSD 25 all caused hypothermia at 25 C and hyperthermia at 33 C. Reserpine caused hypothermia at lower temperatures but no consistent effect at higher ones, and dinitrophenol, a drug usually thought to have a peripheral action on body temperature, followed the pattern of the others. Hence, in assessing the action of a drug on body temperature, it must be realized that there may be a critical ambient temperature at which the effect is reversed. The agents studied appear to interfere with central body temperature regulation.

Tissue Committees.—A recent symposium, reported in *Canadian Doctor* (**24**:29, 1958) without naming the participants, dealt with the question of whether the hospital tissue committee is worth while. The two basic objectives of such committees are the preservation of the integrity of the medical profession and the protection of patients against needless operations. Such committees lack jurisdiction and are strictly fact-finding bodies giving information to the hospital staff. The gynecologist and the surgeon contributing to the symposium agreed that the committee was necessary in smaller hospitals lacking the censorship imposed by the presence of interns, residents, students, and department heads and thought that its presence also made for a more careful recording of cases. It might also be of value where a colleague was in difficulties because of emotional instability, illness, or too great responsibility. The pathologist urged that evaluation of cases should take place within a matter of hours and that surgeons should not be criticized because of the committee's low rating on a specific type of case. The only value of the statistics was to show comparative trends. The lawyer warned of the legal hazards of condemnation of a surgeon's work by a tissue committee. In a malpractice suit a client's lawyer would be in a strong position if he were aware of such condemnation, and since the tissue committee's reports were hospital documents, they could be subpoenaed. The surgeon should have a chance of explaining to the committee the factors that influenced his decision to operate.

Death Rates and Living Standards.—Metropolitan Life Insurance Company figures show that the death rate in Canada for 1958 was the lowest on record—about 8 per 1,000. This decrease in the death rate reflects in large measure the lower incidence of respiratory diseases and to some extent the lower mortality from chronic diseases in elderly people. Cardiovascular and childhood diseases had a lower rate, and the rate for cancer and motor accidents remained about the same as in 1957. The Salk vaccine helped to reduce the number of poliomyelitis cases to fewer than 300 (mostly in Manitoba) as against 9,000 in 1953. However, as a correspondent in *Canadian Doctor* pointed out, the age-adjusted death rates in both Canada and the United States were higher than in Norway, the Netherlands, and Denmark for males, and the Netherlands and Sweden for females. This correspondent speculated on the paradox that the two countries with the highest standards of living in the world do not keep their citizens alive to enjoy it for as long as persons in slightly less favored countries.

Imipramine in Depressions.—Imipramine or N-3′-dimethylaminopropyl-iminodibenzyl hydrochloride was used to treat 84 patients with dysphoric depression at Verdun Psychiatric Hospital, Quebec, by Lehmann and co-workers (*Canad. Psychiat. A. J.* **3**:155, 1958). Their results were roughly comparable to those reported by Kuhn (Switzerland), namely recovery or marked improvement in 30% after two weeks' therapy, and in 60% after eight weeks' therapy. The results were less favorable in patients who had depression associated with neuroses, schizophrenia, or organic conditions than in those with endogenous depression. The dosage usually began at 100 mg. daily by mouth or intramuscularly (both were equally effective) and was increased after a few days to 150 mg. and in a large percentage to from 200 to 600 mg. The incidence of side-effects increased with doses over 200 mg. a day, especially in patients over 65 years of age. The main one was disturbance of autonomic nerv-

ous system function, but there were a few cases of toxic confusion, two of epilepsy, and one of mild jaundice.

Acute Alcoholism.—Kofman and co-workers (*Canad. M. A. J.* **79**:988, 1958) compared the results of treating 500 patients in a state of acute alcoholic intoxication by giving insulin and dextrose intravenously with those in 163 treated with reserpine and 114 treated with perphenazine. Only a few in the series had delirium tremens. Reserpine was given intramuscularly in 2.5-mg. doses on admission and after one hour and then routinely in six hours, with further doses if the patient remained unsettled. An initial dose of 10 mg. of perphenazine was given intramuscularly and repeated after one hour with subsequent 5-mg. doses as needed. Both reserpine and perphenazine were more effective than the insulin-dextrose regimen, and perphenazine was considered the most effective and least complex agent these workers had used in treating acute alcoholism.

FINLAND

Corticosteroid-Produced Peptic Ulcers.—Heino Laitinen, and co-workers (*Acta rheumatol. scandinav.* **4**:205-217, 1958) reported a series of 15 patients with peptic ulcers occurring during corticosteroid therapy which were characterized by a location near the pylorus; large, deep, and often penetrating ulcer niches; mild clinical symptoms; good clinical and roentgenologic healing, even in 7 patients in whom corticosteroid therapy was continued; and absence of late complications, which are not unusual in connection with ulcers at or near the pylorus. The follow-up period was over one year in eight cases, and four years in one. During this time examinations showed an apparently permanent healing. The roentgenograms disclosed either normal conditions or minimal bulbar deformity. Pyloric stenosis, which frequently results from a juxtapyloric ulcer, was not encountered in any of these patients.

Mast Cells in the Gastric Mucosa.—The mast cell count was determined in specimens taken from the fundus of the stomach by the suction biopsy method and reported on by Siurala and Sundberg (*Ann. med. exper. et biol. Fenniae* **36**:271-277, 1958). The mean mast cell count in 17 persons with a normal gastric mucosa was 79 ± 8.6. In 8 patients with superficial gastritis it was 125 ± 24.1; in 21 with slight atrophic gastritis it was 153 ± 18.3; and in 11 with severe atrophic gastritis it was 150 ± 13.7. The difference in the mast cell count of a normal and atrophic mucosa was statistically significant. There was also some correlation between the mast cell count and the degree of inflammatory changes. It could not be demonstrated that the age of the patient or the severity of the disease had any definite influence on the mast cell count of the gastric mucosa.

Asian Influenza.—Ohela and Kaipainen (*Nord. med.* **60**:1700-1701, Nov. 27, 1958) reported that the Asian influenza epidemic was well started in Finland by the end of September, 1957, but by December the number of new cases began to decrease. The total number of cases was estimated to be at least 700,000. Of the 1,322 persons who died in the epidemic, influenza was the sole cause of death in 478 and in the rest one or more additional diseases were involved. A large proportion of the fatal cases were in patients under 5 and over 65 years of age.

FRANCE

Tomography of the Prostate.—Sichel and Blum (*Journal de radiologie, d'électrologie et de médecine nucléaire*, September, 1958) made tomograms of the prostate by taking negatives at depth intervals of 0.5 to 1 cm. If an adenoma is present, its volume and outline can be determined. In case of cancer, the appearance of the dome of the tumor resembles that of the adenoma but is of greater density.

Deaths from Chloramphenicol.—Lamy and coworkers presented to the Académie Nationale de Médecine a series of three cases of fatal purpura hemorrhagia in children who were given small repeated doses of chloramphenicol. They developed a severe thrombopenia against which corticotherapy was of no avail. The authors believe that the small repeated doses caused the development of an allergic phenomenon. They suggested that unless strong indications exist chloramphenicol should not be prescribed.

Humoral Study of Psychopaths.—G. Sandor and C. Chatagnon studied the serums of 230 psychopathic female patients and reported their results at a meeting of the Académie Nationale de Médecine. Of 43 patients with organic lesions, 11 had a normal serum and 22 had hyper-alpha-globulinemia. The findings in 56 patients with acute depression but no organic lesions were similar. In 24 mentally defective subjects, on the other hand, hyper-alpha-globulinemia was rare but 12 of them had hypergamma-globulinemia. The findings in 54 schizophrenics were similar. The authors contrasted the two groups—patients with the organic psychopathy and those with acute depression showing an increase in psychic tension and schizophrenics and mental defectives showing a decrease in this tension. They believed that this tension is associated with a hormonal secretion, which modifies the pro-

tein composition of the serum. The neurohormonal action of the anterior lobe of the pituitary may play a part in the production of hyper-gamma-globulinemia, when the nervous tension falls. Gleye and Sandor showed that epinephrine produced in guinea pigs a marked hyper-alpha-globulinemia. It is therefore possible that psychic tension may provoke the secretion of the adrenal medulla.

NORWAY

Primary Dislocation of the Patella.—As a plea for operative instead of conservative treatment for primary dislocation of the patella, Dr. Y. Kjelstrup (*Nordisk medicin*, Dec. 18, 1958) gave an account of nine such patients operated on by him. Serving as informal controls were six patients who, in the same period, had a history of an earlier dislocation of the patella for which no operation had been performed. All of them were much embarrassed by their knees, which in two cases presented marginal fractures. Of the nine primary cases six patients were under 18. Six of the patients came to the hospital with the injured knee flexed and the patella displaced inwards. On operation, inspection of the joint revealed nothing amiss with it apart from the patella and its attachments. The lesions were varied but more or less rupture of the attachment of the vastus medialis tendon was common to all. After suture of the torn structures the knee was slightly immobilized by a bandage which allowed daily inspection and control of the knee. After about a fortnight, movements were permitted, and after three weeks, walking with crutches. With one exception a complete return to normal was achieved.

Nilatil for Angina Pectoris.—At the Aker and Ullevaal hospitals in Oslo, trials were made with nilatil (amino-ethyl-nitrate-p-toluol-sulfonate) in 58 patients who had angina pectoris. Rörvik and Selvaag (*Tidsskrift for den norske lægeforening*, Dec. 15, 1958) reported that this drug is slower to take effect than nitroglycerine, but its action lasts longer—at least two hours. It reduces the systolic blood pressure by 15 to 20 mm. Hg, and its administration can be sublingual or peroral. It is easily soluble in water, and it keeps well for at least a year in tablet form or solution. Within 10 to 15 minutes it provokes a sense of heat and throbbing in the head and, if the dose is big enough, a headache. This headache was the only important side-effect, and it was taken as a therapeutic guide, pushing the dose up to a point just short of the headache level. The usual dosage was one 2-mg. tablet three or four times a day. Headache was a guide to a reduction of the dosage, but there were only two patients in whom headache led to discontinuation of this treatment. As excellent or marked relief of symptoms was obtained in about 67% of their patients, the authors concluded that nilatil was the best slow-acting nitrate derivative available for angina pectoris.

Asian Influenza.—Dr. A. Harboe of the Influenza Laboratory of the State Institute for National Health in Oslo (*Nordisk medicin*, Nov. 27, 1958) reported that the outbreak of Asian influenza started in Rjukan, a small inland town, towards the end of August, 1957. Samples received by his laboratory on Sept. 9 were the first to contain the causative virus. In the middle of September there was an intense outbreak of the disease in army concentrations in Stavanger, and in the course of the next fortnight it spread to most of the military centers in southern Norway. Ultimately the whole of Norway was involved, and 19 different strains were cultivated. The major wave, involving the whole country in the first half of October, was followed by a second wave in Oslo at Christmas. School children and the personnel of military camps showed a particularly high morbidity, and in a camp of 223 recruits 88% were found to have developed antibodies to the virus. In the adult general population in Oslo, the incidence of influenza was between 10 and 15%. After isolation and typing, the different strains were sent to the World Influenza Center in London where they were identified as belonging to the Asian type. In Norway no difference could be found between the Norwegian strains and the prototype Singapore strain in respect to their antigenic properties. Vaccine imported from Denmark and Holland was used in the isolation departments of the larger hospitals. It was calculated that at Oslo's City Hospital vaccination had reduced the number of cases by 50% and the number of sickness days by 60%.

Enuresis.—A note of disillusion over the hospital treatment of nocturnal enuresis was struck by Rinvik and Steel (*Tidsskrift for den norske lægeforening*, Dec. 15, 1958) who treated 186 patients with this condition in a children's hospital. A questionnaire addressed to the parents after discharge from the hospital yielded answers from 122. They showed that a recovery could be claimed in 20%, and some improvement in 17%, whereas in the remaining 63% the enuresis persisted one to six years after discharge. Little use was made of drugs in the hospital where the children were awakened once nightly to empty their bladders. One of the main arguments in favor of hospital treatment for enuresis was the opportunity it afforded for the discovery of organic and mental disease. Various tests were applied, including urography, which in 9 of the 158 patients thus examined showed abnormalities of the urinary tract. There were also 12 cases of men- 50% one or more members of the family also suffered retardation. The 122 answers showed that in fered from enuresis. The authors concluded that

little can be gained by admitting patients under 5 or 6 years to the hospital even though organic disease can thereby be detected earlier. They are skeptical about the value of reducing the water intake in the afternoon, for the children are quick to circumvent their nurses in this respect. As for drugs, tincture of belladonna continues to have its advocates, but it must be pushed if it is to be effective.

SWEDEN

Radical Pancreatic Surgery.—Erik Millbourn (*Acta chir. scandinav.* **116**:1, 1958) performed a radical pancreatectomy on 15 patients with cancer of the head of the pancreas and 1 with cancer of the ampulla of Vater. There were three operative deaths, two of which occurred early in the series. Advanced age (over 70 years) in four patients was not considered a contraindication to this operation. Two patients including one with carcinoma of the ampulla of Vater survived almost four years. Two survived two and one-half years. Two patients felt well and had no signs of metastasis or recurrence when last seen three and one-half and two and one-half years, respectively, after the operation. One patient had a second operation, a pancreaticogastrostomy, in March, 1958, after which he had no evidence of metastasis or recurrence. The average survival time was 23 months. Radical pancreatectomy gave these patients their only chance of survival. The author recommended pancreaticoduodenal resection, combined with the necessary anastomosis, in patients with cancer of the head of the pancreas or of the ampulla of Vater, where local excision via a duodenotomy is not possible. He preferred pancreaticogastrostomy to pancreaticojejunostomy, and stated that total pancreaticoduodenectomy was to be avoided.

The author outlined a two-stage operation, the first stage consisting of cholecystojejunostomy and enteroanastomosis and the second stage, pancreaticoduodenal resection, pancreaticogastrostomy, choledochojejunostomy, and gastrojejunostomy. The gastrojejunostomy must be placed distally to the other anastomosis on the efferent loop. Most of the patients are thus provided with two sphincterless openings for the bile flow to the jejunum, a cholecystojejunostomy established in the first stage and a choledochojejunostomy in the second. The coexistence of the two sphincterless openings for bile flow into the jejunum does not as a rule produce postoperative complications. Of eight patients with two openings one had trouble postoperatively, probably due partly to the fact that one sphincterless opening is all that is necessary for the bile flow to the jejunum. One patient, who subsequently died of peritoneal carcinosis, had attacks of cholangitis in the last months of her life. In patients with carcinoma in the ampulla a biopsy specimen should be taken in the first stage through duodenotomy. In those with carcinoma of the head of the pancreas excision of tissue for biopsy is not always without danger. In addition, it is sometimes difficult for the surgeon to obtain a satisfactory biopsy specimen.

Treatment of Ureterolithiasis.—In 1956 Einar Sandegård analyzed a series of patients with ureteral stones treated expectantly and in *Acta chirurgica scandinavica* (**116**:52, 1958) he presented a follow-up examination of a similar series five years after the attack. Of these 94% were examined urographically. In the interval of between five and six years from onset to follow-up definite recurrences were found in 17% and probable or possible recurrences in 8%. The roentgenographic follow-up demonstrated a recurrence of renal calculi in only 4%. Thus, although ureteral recurrences were fairly common after ureterolithiasis, concretions were rarely found in the kidney. In all of 86 patients treated conservatively, follow-up urography showed the excretory function of the kidneys to be normal. In 29 treated with active procedures, appreciable renal damage had been present prior to operation in 3 but the remaining 26 showed normal kidney function on urographic follow-up examination. No new lesions such as dilatation of the ureter or renal pelvis were noted.

Combined Tetanus Prophylaxis.—The effect of combined active-passive prophylaxis against tetanus was compared by Bergentz and Philipson (*Acta chir. scandinav.* **116**:58-67, 1958) with that of solely passive and solely active immunization by determining the serum antitoxin concentrations in military recruits at different periods after immunization. The effect of a booster dose was compared in the same way in the groups treated with active and combined immunization respectively. The results on 22 subjects with passive immunization only, 19 with combined simultaneous active-passive immunization, and 20 with active immunization only led to the following conclusions: The passive immunity secured by combined treatment was slightly lower than that of passive treatment. Of those immunized passively 60% had titers above 0.2 immunizing units (IU) per milliliter but only 15% of the simultaneously immunized had titers above that level. Corresponding values for the 0.1 IU per milliliter–level were 86 and 68% respectively. Measurable antitoxin concentrations corresponding to active immunity in the serums of those treated with simultaneous prophylaxis appeared later than in those actively immunized. A rise in antibodies was not detected until 45 to 74 days after injection in subjects receiving combined treatment while the rise in antibodies appeared between 14 and 24 days after injection in the group actively immu-

nized. The effect of a booster dose was the same in the group immunized actively and in that treated with a combined injection.

Tennis Leg.—Tennis leg is a traumatic lesion of the calf which is generally believed to be due to a subcutaneous rupture of the plantaris muscle. Arner and Lindholm (*Acta chir. scandinav.* **116:**73-75, 1958) questioned whether the signs and symptoms of tennis leg were caused by such a rupture. The location of the pain, the distinct tenderness and hematoma formation on the medial aspect of the calf midway between the heel and the knee, and the loss of power could not be accounted for by rupture of the plantaris muscle belly, its musculotendinous junction, or the tendon itself. Twenty patients with characteristic features of tennis leg were studied. A gap in the medial gastrocnemius belly roughly at the musculotendinous junction was observed in every instance. Surgical exploration in five verified the rupture of the gastrocnemius, while the plantaris tendon was found to be intact in all five. In all 20 patients the rupture was shown to occur on sudden dorsiflexion of a foot in supination and plantar flexion with the knee joint in extension. This combination of movements produces the greatest contraction of the medial gastrocnemius belly thereby exposing it to the greatest indirect violence with resultant rupture.

SWITZERLAND

Exports of Narcotics.—The permanent Central Opium Board (Geneva) drew attention in a report to the obligations of governments in connection with the export and import of dangerous narcotics. Specific reference was made to the West German production of normethadone, a narcotic described as being as dangerous as morphine, and used in such cough mixtures as Ticarda and Taurocolo. This drug is manufactured mainly in West Germany and has been under international control since November, 1954, although Bonn, not being a party to the 1948 protocol, has not exercised any control over it. The West German government failed to report its exports of normethadone for 1957 to the Central Opium Board, although there was evidence that in 1956 preparations of this narcotic had been exported to 56 countries 48 of which did not report the fact when questioned. Some of the governments concerned stated that the importation took place without their knowledge.

The Board blamed the failure to disclose this information on the governments concerned. It strongly recommended that, when any new product for which analgesic or antitussive properties are claimed is about to be marketed, the government of the country of manufacture should subject it to control measures until the World Health Organization has determined its liability to habit formation. The Board stated that the guiding principle in all such cases should be that commercial interests must yield to consideration of public health. After the issue of the Board's report it was stated that the Interior Ministry of West Germany would introduce further legislation for the control of narcotics. The Central Opium Board gave the following data on world narcotics production: In 1957 714 tons of raw opium were produced, less than the average annual production of 867 tons during the period from 1946 to 1957; morphine production was 109 tons, of which 94 tons was used for the manufacture of codeine and other derivatives. The consumption of morphine as such was only 4 tons. The production of codeine was 97 tons, an increase over previous years, of which 90 tons was consumed and the remainder converted into other derivatives.

Of the synthetic narcotics meperidine still leads the field with an annual consumption of 14 tons. The use of cocaine is declining. Annual consumption is now 1,619 kg., a reduction of nearly 400 kg. in three years. The consumption of methadone dropped from 750 kg. in 1954 to 464 kg. in 1957. The Board stated that North America continued to be one of the main destinations of illicit narcotic traffic, particularly in heroin. Much traffic in marijuana occurred in Africa, although attempts have been made to stamp it out in Egypt where several confiscations have been reported. An active illicit drug traffic, particularly in opium, morphine, heroin, and marijuana, occurred in the Near East. In the Far East illicit traffic in these narcotics continued in Hong Kong, Singapore, Malaya, Thailand, and China. There was also illicit opium traffic in Pakistan, India, and Iran.

UNITED KINGDOM

Maple Syrup Disease.—The first British case of a rare disease known as maple syrup disease was observed by Mackenzie and Woolf (*Brit. M. J.* **1:**90, 1959). The condition is so called because the urine has the odor of maple syrup. The patient was a 4-month-old girl with anemia, lack of control of head movement, increased muscle tone and tendon reflexes, pallor of the optic disks, a low mentality, and an abnormal electroencephalogram. When the urine was examined to exclude phenylketonuria it was found to smell of maple syrup. On two-dimensional paper chromatography valine, leucine, and isoleucine were found in large amounts. They were also present in excess in the blood, spinal fluid, and saliva. The urine contained large quantities of keto acids and alpha-hydroxy acids, which were responsible for the smell of maple syrup. This was intensified by acidification with sulfuric acid. Further examination revealed the presence of large amounts of indolylacetic and indolyllactic acids. The fasting blood sugar level was only 52 mg. per 100 ml.

Another case was observed simultaneously in New York by Dancis and co-workers (*Brit. M. J.* 1:91, 1959). Maple syrup urine disease is an inborn error of metabolism, involving valine, leucine, and isoleucine and similar in some respects to phenylketonuria, for which it may be mistaken as results of the ferric chloride test are similar for both. In both conditions there is a disturbance of tryptophan metabolism as shown by the excretion of large quantities of indolylacetic and indolyllactic acids. Like phenylketonuria the condition is associated with progressive mental deterioration. Mackenzie and Woolf gave the child a diet low in valine, leucine, and isoleucine, but the mental deterioration was such that improvement was unlikely. They considered that the accumulation of abnormal metabolites, i. e., the hydroxy and keto acids, and the amino acid concentration in the blood were responsible for the mental defect.

Reasons for Shortage of Nurses.—British hospitals are finding it increasingly difficult to maintain a 24-hour nursing service. One difficulty is the provision of adequate night service. The Royal College of Nursing, reporting on the problem, deplored the practice in many hospitals of waking patients at 5 a. m. Because of this, night nurses are expected to do far too much work in the early hours of the morning, and in consequence they suffer from overfatigue and the quality of their work deteriorates. The anxiety associated with night duty causes many student nurses to abandon their careers. The report urged the reduction of night duty from 12 to 8 hours. Other recommendations were two meal breaks away from the wards and advance notice of nights off so that the nurses can join in the social life of the community. Junior nurses should not be left alone when seniors go to meals, and trained nurses should not have to undertake domestic and clerical duties as many of them do at present. Salaries should be adequate. The report recommends that nurses should not do more than two years of continuous night duty.

Air Pollution.—Stocks (*Brit. M. J.* 1:74, 1959) observed that when standardized mortality ratios for bronchitis and cancer in the towns of England and Wales were related to the average amounts of undissolved deposit and smoke from the air, highly significant statistical correlations were found with both types of pollution, after eliminating the effects of population density on the correlations. Data were obtained from 58 towns in the industrial areas of Lancashire and Yorkshire. Air pollution was measured by the "deposit index," or monthly average number of grams of undissolved matter deposited per 100 sq. m. of surface, and the "smoke index," which was measured by drawing a known volume of air continuously through a white filter paper for a given time. The darkness of the stain produced was matched with a standard scale and expressed in milligrams per 100 cu. m. of air. The data were averaged over a period of 10 years. Deaths from bronchitis and cancer of the lung, bronchus, stomach, intestine, rectum, and breast were obtained from the statistical reviews of each area over the last five years.

In all areas examined bronchitis was significantly correlated with atmospheric deposit but not smoke, whereas for lung cancer the reverse was true. In Lancashire lung cancer was strongly correlated with population density and this appeared to confirm the effect of wind-borne smoke on the incidence of the disease. The mortality from cancer of the stomach was related significantly to both deposit and smoke in the urban areas, whereas breast cancer showed no correlation with air pollution. The most likely explanation of this is the exposure of food to dirty air. This view received some support from the fact that in the United States, where the wrapping of food was obligatory long before it was in Britain, death rates from gastric cancer have fallen steadily, whereas in Britain they have not. The correlation of intestinal cancer with atmospheric deposit and smoke was below the conventional level of significance.

Medical Honors.—Included in the list of New Year's Honors are Prof. Arthur P. Thomson, this year's President of the British Medical Association, professor of therapeutics, and dean of the faculty of medicine at the University of Birmingham; Dr. Arthur W. Morrow, physician at the Royal Prince Alfred Hospital in Sydney; and Dr. Milton A. Margai, who has been Premier of Sierra Leone since last summer. A knighthood was also conferred on Prof. A. W. Ewing, director of the department of education of the deaf at the University of Manchester.

Politics in Medicine.—Sir Walter F. Hannay, a Harley Street physician, writing in the *Daily Telegraph* of Dec. 2 deplored the intrusion in the last decade of party politics into the realm of medical science and blamed this intrusion for the present retardation in the advance of medical knowledge in Great Britain. The Imperial Cancer Research Fund, a body supported entirely by voluntary contributions, with no political affiliations, must exist on a meager annual budget of $349,510. This brilliant team of scientific workers has absolute intellectual freedom to pursue its investigations, but is sadly hampered by lack of funds. On the other hand, the government-sponsored Medical Research Council has an annual grant of $61,500,000. The 1955-1956 report of this body covered 270 pages of which 210 were devoted to listing the names of the distinguished scientific personnel and only 56 to the work done during the year. The reported findings of the Council made very indifferent read-

ing, and the taxpayer must speculate on the advantages of so costly an association of research workers. This was cited as one more indication of the paralyzing effect of the politician's encroachment into medical science.

Infant Deaths a Mystery.—Mothers have been blamed unjustly or have erroneously thought themselves at fault when apparently healthy children have been found dead in cots. An expert committee, investigating sudden deaths in infancy, has found them innocent of negligence. A member of the committee, Dr. D. M. T. Gairdner, consultant pediatrician, Addenbrooke's Hospital, Cambridge, speaking at a British Medical Association meeting in Southampton, said no evidence that mechanical asphyxiation played an appreciable part in these deaths was found. This is of great comfort to the mothers. Since the cause of these deaths is still unknown, no suggestions as to their prevention can be given. The inquiry lasted over four years; the sudden deaths of 81 children (53 boys and 28 girls) aged 2 weeks to 2 years, or 23% of all deaths in this age group in the areas studied, were investigated.

If this sample was typical, it meant that 1,600 such deaths occurred in England and Wales yearly. These deaths were rare in infants under 1 month and reached a peak in those of 4 months of age; 58 occurred in the six-month periods between November and April. Only seven babies were found lying face down. Mothers at first said that all the children were perfectly well, but inquiry showed that 11 had been seen by a doctor in the three days preceding death and 54 had had trivial symptoms. Autopsies held after 92 such deaths established the cause in only 23. Both breast-fed and bottle-fed babies were involved. The seasonal incidence supported the theory that infection played some part. Dr. Gairdner concluded that mothers should still be advised not to give babies soft pillows because occasionally babies do bury their heads in the bedding.

The Mental Health Bill.—The government's Mental Health Bill is discussed in an annotation in the *British Medical Journal* of Jan. 10. The Bill appeared about 18 months after the report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency and embodied nearly all the important changes recommended by the royal commission and by the British Medical Association's Psychological Medicine Group Committee. As a result of the detailed examination the bill will receive in Parliament no doubt many minor changes will be made in it, but as it stands it represents a notable administrative advance in the care of the mentally ill. Mental health review tribunals are to be set up in the areas of regional hospital boards to consider applications from patients and relatives for their release from hospital. The single term "mental disorder" is to cover all forms of mental illness or disability, and arrangements can be made for any kind of hospital to receive any type of mental patient, whether on an informal basis or under detention. The bill will remove all the formalities which under the present law must be observed before even a voluntary patient can enter a mental hospital, but, in their own interests or for the protection of others, some mentally disordered patients, as in the past, will be compulsorily admitted to hospital and detained therein.

The four groups of mentally disordered patients who may require compulsory detention are the mentally ill, subnormal, severely subnormal, and psychopathic. The terms "mental defective," "idiot," "imbecile," and "moral defective" will no longer be used. Severe subnormality means a state of arrested mental development which renders the patient incapable of living an independent life. Subnormality means a state of arrested mental development which requires or is responsive to medical treatment. Psychopathic disorder means a persistent disorder of personality which results in abnormally aggressive or seriously irresponsible conduct on the part of the patient and requires or is responsive to medical treatment. Patients may be compulsorily admitted to hospital for observation or treatment. In both cases the application will have to be supported by two medical recommendations, one of these by a psychiatrist.

Whether or not the changes brought about by the bill will be notably and quickly advantageous to patients will depend on the attitude of the public to mental illness. The social adaptation of patients discharged from mental hospitals is often precarious. They and their families can receive much-needed support from the aftercare services provided by the hospital and local authorities, but without education of the general public the way may still be hard for those who are trying to overcome a serious disability.

Opposition to "No Strike" Report.—The British Medical Association Council claims that physicians may, under great provocation, be justified in a mass withdrawal from the National Health Service (NHS). This is often referred to in the lay press as going on strike. This is a misrepresentation of what might, in rare circumstances, happen, because physicians would continue to see patients. Sir Frank Newsam, formerly Permanent Undersecretary of State at the Home Office, was commissioned by the General Medical Services Committee, which is representative of the general practitioners who work in the NHS, to investigate the problems and frustrations of the 22,000 family physicians within the NHS and to suggest other ways in which a health service might be organized. The committee wanted an independent inquiry by someone of some eminence. It forwarded Sir Frank's report to the Council of the BMA and the *British Medical Journal* published it with a

statement by the Council in the *British Medical Journal* of Jan. 17. The Council strongly criticized the report, asserting that Sir Frank had completely balked the issue he was instructed to grapple with. Although he failed to suggest any alternative schemes his report is not without value. Its value lies in the warning given to the profession that a "strike" would result in a fully salaried NHS. The Council is at this stage refraining from detailed comment, limiting itself to admitting the value of negotiation and the belief that the medical profession, faced with a serious challenge to its principles and traditions, might be compelled to contemplate withdrawal from the NHS.

Sympathectomy for Hypertension.—Newcombe and co-workers of Leeds (*British Medical Journal*, Jan. 17, 1959) reported a series of 212 patients who underwent sympathectomy for hypertension 4 to 10 years earlier. The operative mortality was 4%. The survival rate of 76% for five or more years agrees with other published records of patients treated by sympathectomy and is in favorable contrast to any published account of a series of patients treated conservatively. A sustained reduction of diastolic pressure of more than 20 mm. Hg occurred in 27%. Retinal improvement occurred in 49% of those with severe changes, and when there was no improvement in advanced retinal degeneration death was not long delayed. Symptomatic relief after sympathectomy was the rule. Reduction of blood pressure, if only for a few months, may prevent malignant hypertension. Sympathectomy in hypertension gives many patients an increased expectation of a full and active life.

Menstruation and Acute Psychiatric Illness.—Investigating the time of hospitalization of 276 women with psychiatric disease Dalton (*Brit. M. J.* **1**:148, 1959) found that 46% of admissions occurred during or just before menstruation and that 53% of attempted suicides took place during menstruation; successful suicides were more common during the luteal phase. Of patients with depression and of those with schizophrenia 47% were hospitalized during or just before menstruation. The significance of these figures lies in their prognostic value. Psychiatric patients who first seek advice in the premenstruum may be expected to get worse up to the third or fourth day of the menstrual cycle. Premenstrual tension can be successfully treated whether it occurs alone or in association with psychiatric illnesses and regardless of whether the hormonal changes of menstruation cause or precipitate the onset of an acute psychiatric episode. The influence of menstruation on psychiatric admissions was evenly distributed among single, married, and widowed women; among the nulliparous and multiparous; and among those admitted for first and recurrent attacks. There was, however, a marked difference in age. The disturbing influence of menstruation was greatest among those under 25 years of age. Depressive and suicidal patients were evenly distributed among all ages, while schizophrenia was commonest in the youngest age groups. The remaining patients suffered from a wide variety of psychiatric conditions including psychoses, alcoholism, psychopathic disorders, and neurosyphilis. The dates of their admissions were evenly distributed throughout the menstrual cycle.

Bulletin on Rheumatism.—Family doctors throughout Britain now receive a quarterly report on the latest advances in the treatment of rheumatic diseases issued by the Empire Rheumatism Council. The first of these reports was an introductory document in which Dr. W. S. C. Copeman, chairman of the Council, stated that chronic gout has become increasingly common in the last few years.

Spontaneous Improvement in Psychoneuroses.—In assessing the value of any form of therapy it is important to know the degree of spontaneous recovery to be expected from the untreated patient. Wallace and Whyte (*Brit. M. J.* **1**:144, 1959) studied the natural history of untreated psychoneuroses in 49 psychoneurotic patients who would normally have had treatment but for various reasons did not. The patients were classified as recovered, improved, or not improved after follow-up periods of three to seven years. Some improvement was noted in 32 (65.3%). Any recovery that occurred spontaneously did so by the third year. The better-integrated patients showed a higher recovery rate and a greater capacity for adjusting to adverse and difficult circumstances. Factors associated with improvement were a helpful marriage partner, adequate housing, good personality, success in work, general adequacy in life situations, and participation in group activities. This high spontaneous recovery and improvement rate must be borne in mind when assessing the value of any new form of treatment, whether by drugs, psychotherapy, or physical methods.

Zollinger-Ellison Syndrome.—Further cases of the recently described Zollinger-Ellison syndrome were reported by Summerskill and Pender (*Lancet* **1**:120, 123, 1959). This syndrome is characterized by gastric hypersecretion, fulminating atypical peptic ulceration, and pancreatic islet cell hyperplasia. Diagnosis is usually made retrospectively after gastric operation or at autopsy. Summerskill reported a case diagnosed before operation. The patient had jejunal ulcers and secreted over 500 ml. of gastric fluid hourly with practically no response to histamine stimulation. Acid-pepsin activity was present in the jejunum. Diarrhea and steatorrhea were prominent clinical features. Fat digestion in the jejunum was depressed by the presence of acid, and this caused the steatorrhea and diarrhea. Pender's patient had an islet cell tumor of

the pancreas. The patient's daughter also had a benign islet cell adenoma. The patient had had repeated but unsuccessful operations for recurrent peptic ulcers. Eventually treatment by total gastrectomy and removal of the benign islet cell tumor resulted in improvement.

Poliomyelitis Vaccine.—An electron microscope will speed the search for a poliomyelitis vaccine produced without the use of monkeys. This and an analytic centrifuge will be bought by the National Fund for Poliomyelitis Research. Britain and the United States together use nearly 30,000 monkeys a month for producing and testing vaccine, and other countries are entering the production field. Research workers feel that in time the demand for monkeys may outstrip the supply. Each monkey yields about 700 doses of vaccine and costs the manufacturer about $42. There have been difficulties about their export from India, because in some areas monkeys are regarded as sacred animals.

Curtains and Hospital Contamination.—Hughes (*Lancet* 1:152, 1959) studied a 14-bed general surgical ward in an attempt to discover possible causes of wound sepsis. Weekly tests were made from samples of the curtains, which were cotton and of the pull-round type. Staphylococcus pyogenes was isolated from 54% of 250 samples. On one occasion clean curtains, which had been through a high-pressure steam sterilizer, were put up around the bed of a patient who had a staphylococcic wound infection of known bacteriophage type. In less than 24 hours the same bacteriophage type of staphylococci was isolated in large numbers from the curtains.

Health of School Children.—In his report on the School Health Service (The Health of the School Child, Her Majesty's Stationery Office, 1959) Sir John Charles, Chief Medical Officer of the Ministry of Education, stated that one of the main health problems in children is overnutrition and not malnutrition. He blamed too many candies, chocolates, ices, and cookies and too much carbohydrate in the diet. On the credit side, boys and girls are taller, heavier, better clad and shod, and cleaner than they were 50 years ago. They reach physical maturity earlier and may expect to live 20 years longer. Tuberculosis, rickets, and rheumatism in children have been virtually eliminated. Most cases of crippling and deformity are now congenital. More children die from accidents than from disease. Traffic accidents are the cause of half the deaths in children, and many of these occur when children are going home from school. Children should be told about the risk of lung cancer from smoking cigarettes as many school children smoke. An inquiry among 300 boys and girls in a high school on the Isle of Wight revealed that 30% of the boys and 15% of the girls were regular smokers. Increased consumption of candies and chocolate was blamed for the increase in dental decay in children. The school medical service is devoting more attention to emotionally disturbed and delinquent children. The number of children appearing in the juvenile courts has increased in 25 years from 13,000 to 38,000 annually. The school medical service now covers 6,500,000 children in 30,000 schools and more than 2,000,000 have an annual medical examination.

New Deal for Midwives.—The Minister of Health proposed a new deal for midwives to meet the serious shortage in the hospital and private midwife service. Among the recommendations made was the employment by the maternity services of more auxiliary nursing and domestic staff to enable midwives and midwives in training to get on with their professional work. It was also suggested that midwives should have responsibility for individual patients throughout the patients' stay in hospital. New maternity hospitals should be planned with this end in view. Unnecessary rules and restrictions should not be applied to pupil midwives, particularly when off duty, and they should have better opportunities for training than at present. Provision should be made for training women who have no nursing qualifications as midwives. The satisfaction the midwife gets from her work could be increased by inculcating a more appropriate mental attitude in patients and their relatives toward her profession.

Radioactive Fall-out and Leukemia.—An investigation is being carried out by the Lancashire Health Committee into the cause of the reputed increase in deaths from leukemia and aplastic anemia in the district and its possible association with the radioactive fall-out that occurred at Windscale, Cumberland, in October, 1957. A plutonium plant became overheated and quantities of fission products, including radioactive iodine (I^{131}) contaminated the surrounding countryside. It is reported that several young people in the area have died from aplastic anemia. The local health officer is conducting the investigation. All county health officials have been asked to report cases of leukemia and aplastic anemia. Medical Research Council experts think it unlikely that the Windscale accident is linked with deaths from leukemia or aplastic anemia. The major component of the fall-out was I^{131}, which has never been linked with leukemia or aplastic anemia. Neoplastic changes after irradiation do not occur until many years after exposure. As leukemia is rare fluctuations may occur from time to time in any area.

CORRESPONDENCE

ANTIBIOTIC LOZENGES

To the Editor:—In the past few years I have seen a fairly large number of patients who have complained of severe sore throat after using antibiotic lozenges. This was due to infection caused by Candida albicans. In all of these patients the soft palate and pharynx were extremely red. In some there were small white patches indicating the presence of colonies of C. albicans. The pain is more severe in this condition than in that associated with any of the inflammatory diseases of the mouth and throat, including severe streptococcic infections. There have been cases of prolonged illness and even death from this cause. For some time I have questioned the moral and legal right of the manufacturer to market a product so injurious to health and at times to life itself. About 25 different antibiotic lozenges are offered for sale. Some contain more antibiotics than others. At least two are advertised extensively on radio and television.

Following is a list of antibiotic lozenges which are sold on prescription or over the counter in the average pharmacy.

Single Antibiotic Troches
- Achromycin pharyngets (Lederle)
- Achromycin troches (Lederle)
- Aureomycin pharyngets (Lederle)
- Terramycin troches (Pfizer)
- Bacipharyn (Reed & Carnrick)
- Baci-Troche (Upjohn)
- Teeds lozenges (Warren-Teed)
- Pemzoles lozenges (Pitman-Moore)
- Lozilles (White)
- Tyrosan lozenges (Recsei)

Combined Antibiotic Troches
- Sul-Pondets (Wyeth)
- Bacillets (Abbott)
- Pondets, Penicillin-Bacitracin (Wyeth)
- Candettes (Pfizer)
- Du-Biotic troches (White)
- Orobiotic (White)
- Spectrocin (Squibb)
- Tracinets troches (Merck, Sharpe, & Dohme)
- Wybiotic troches (Wyeth)
- Pentazets troches (Merck, Sharpe, & Dohme)
- Hydrozets (Merck, Sharpe, & Dohme)
- Tetrazets (Merck, Sharpe, & Dohme)
- Isodettes (Isodine)

Penicillin G Crystalline Troches
- Troches with 5,000; 10,000; 20,000; or 25,000 units each (various manufacturers)
- Troches with 5,000 units of crystalline penicillin G with benzocaine
- Troches with 5,000 units of procaine penicillin G

Each of the antibiotic lozenges, regardless of the number used, can permit a Candida infection of the soft palate and pharynx to gain a foothold. If we multiply the several hundred cases which I have seen by the number of family physicians and specialists who have also seen similar cases, the aggregate number and the number of work days lost would be staggering.

The purpose of this letter is to ask what can be done toward a discontinuance of the sale of all antibiotic lozenges. The fact that some physicians prescribe these lozenges cannot be construed as an argument in favor of their use. Many doctors are not aware of the danger involved in using antibiotic lozenges. Unfortunately, few articles have been written by those who have encountered patients with Candida infection of the mouth and throat. Frequently the physician who prescribes the lozenges does not see the patient at the time the severe sore throat develops. Action taken by members of the medical profession could do much to stop this health menace.

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CHLORPROMAZINE JAUNDICE

To the Editor:—I wrote a report on chlorpromazine jaundice, more than two years ago, based on 17 cases (Hollister, *Am. J. Med.* **23**:870, 1957); since that time I have seen only one other case. This declining prevalence of jaundice has also been noted by another observer (Pollack, *Am. J. Psychiat.* **113**:1115, 1957). To provide further information, questionnaires were sent to 67 psychiatrists and mental hospitals using or investigating tranquilizing drugs; 45 replies were received, providing the following data.

In the year preceding the inquiry, 25 of the respondents had encountered at least one case of chlorpromazine jaundice, while 20 had encountered none. Eighty-seven cases of jaundice were reported by these 25 sources, the largest single series being 13 cases. Data were sometimes incomplete in regard to the number of patients treated for the first time with chlorpromazine during the same period. Available data showed that 70 cases of chlorpromazine jaundice had occurred in about 15,000 patients treated, a prevalence of about 0.5%. Of those respondents expressing an opinion, 20 thought that the recent prevalence of chlorpromazine jaundice was lower than that of their previous experience, and 14 thought that it was similar. None thought that it was higher. The customary practice of most clinicians was to discontinue the drug therapy or switch to another if jaundice occurred; only three continued chlorpromazine therapy throughout the episode of jaundice.

Various reasons were given to explain the lowered prevalence of this complication by those who thought such was the case, the most frequently mentioned reason being that current dosage tended to be lower and better controlled because of prior experience. This reason is contrary to the experience of many investigators that the dosage of drug bears little relationship to the production of jaundice. The second most common reason cited was that impurities originally present in the drug had now been removed due to more reliable methods of manufacture. The manufacturer of the compound disclaims this possibility, pointing out that chlorpromazine is a synthetic compound. Also, other phenothiazine derivatives produce similar jaundice, and it is unlikely that all would have the same contaminant. Another idea was that a period of high prevalence of infectious hepatitis could have coincided with the early use of the drug, the latter making patients more susceptible to this illness. Also mentioned were the elimination of patients with known liver disease, the use of alkaline phosphatase determinations as screening during the early phase of treatment, and the fact that many patients may have been previously treated without the knowledge of the physician and thereby "desensitized" to the drug.

Jaundice was reported as a complication of three other phenothiazine derivatives: promazine, mepazine, and prochlorperazine. In the case of the latter drug only one report was received, despite the fact that many of the respondents noted that they were using this drug increasingly. The majority opinion is that chlorpromazine jaundice is a drug allergy. The declining prevalence of this complication with increasing exposure of the population to it is contrary to the usual experience with allergic reactions to drugs. The explanation for this phenomenon is still not clear.

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ELI LILLY MEDICAL RESEARCH FELLOWSHIP (SOUTH AFRICA)

To the Editor:—Medical practitioners who are registered in South Africa and who may at present be in the United States should be aware of the fact that applications may now be submitted for the 1959 award of the Eli Lilly Medical Research Fellowship. The fellowship is for the purpose of research and is not for postgraduate clinical study. The net value of the fellowship is $300 a month for 12 months, plus return traveling expenses to the point of study in the United States of America. Further details can be obtained from the undersigned. The closing date for applications is June 30, 1959.

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MUSEUM OF MEDICAL SCIENCE

To the Editor:—We in the Wellcome Museum of Medical Science have read with great interest the letter by Dr. Frederick Stenn in The Journal (**169**:67-68 [Jan. 3] 1959). To us has been entrusted the task of maintaining the museum of medical science as a teaching institution designed primarily for postgraduate medical men but suitable, also, for undergraduates, nurses, teachers of biology, and their senior students.

The various aspects of medicine now dealt with in this museum are divided on an etiological basis. Thus, we have eight major heads, namely, protozoal diseases, diseases due to bacteria, diseases resulting from viruses, diseases of rickettsial origin, helminthic diseases, fungus diseases, spirochetal diseases, nutrition and malnutrition, and a small section dealing with venomous snakes and arthropods. The method used to describe these conditions is an elaboration of that devised by the original director of this museum, the late Dr. Daukes. The written matter is presented in a synoptic fashion, illustrated by charts, diagrams, pictures, roentgenograms, gross pathological specimens, and photomicrographs illustrating the histological, pathological, entomologic, and parasitological aspects of the conditions described.

Recently the section of the museum dealing with schistosomiasis was shown at a meeting of the South African Medical Association, in Durban, and the section on trypanosomiasis was on display at the Sixth International Congress on Malaria and Tropical Diseases, in Lisbon. The administrative problems in arranging loans are formidable, a matter well appreciated by all museum curators; but on occasion we have been able to supply some material for use by individuals and institutions who have applied to us for assistance.

We do not fully agree with some of the methods of audiovisual instruction proposed by Dr. Stenn. Some of them go against the ancient axiom that clinical medicine can be effectively learned at the bedside and at the bedside only. We have, however, been much interested to see that the concept of using a museum as a main center for medical teaching has found expression in a letter in The Journal. Changes in medical education evolve but slowly. The example and the potentialities of the system followed in the Wellcome Museum of Medical Science have been increasingly appreciated in the United Kingdom during the 45 years of the museum's existence. We shall be greatly interested to see what developments, if any, may take place in the United States as a result of Dr. Stenn's spirited appeal.

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THE LEISURE CORNER

PART-TIME FARMING

Growing things for profit is not quite the same as growing them for fun, but trying to get a profit out of the soil can provide a great deal of pleasure as a part-time hobby for a physician with an independent income. In part-time farming physicians can get away from the complex problems associated with medical practice and find relaxation in what amounts to a completely different occupation. It is possible to trace concrete accomplishments in farming and to realize a sense of progress and gratification.

A part-time farmer owns his own farm and generally lives on it for at least a part of the year. The farm usually starts off being a place for week-ends and summer vacations. Part-time farming is a quite different and more ambitious procedure than tending a garden about one's home. Actually, many of the problems facing the part-time farmer are similar to those confronting the full-time farmer, with one major difference: the part-time farmer does not depend on his hobby to make financial ends meet.

If you have never worked on a farm it is likely that you have some idyllic notions about the kind of life it affords. Returns are not always up to expectations. When you plan to buy a farm make certain it is in a reasonably accessible location. Investigate all phases of farming with the same perspicacity you would apply to evaluating a medical problem. Your first concern should be equipment. Is your back strong enough to do your own plowing, or should you hire someone else to do it? Do you need one or more horses? What equipment should be purchased and what rented? Do you intend to raise fruit? Do you intend to raise chickens and rabbits? These are some of the questions the part-time farmer must answer. Livestock cannot be neglected; someone must always be on hand to keep a close watch. When arrangements are made it is essential to keep an eye on cost.

If you plan to make part-time farming the profitable hobby it can be, it will be necessary, among other things, to investigate the market for cash crops and determine what crops are adapted to your locale and soil. In this connection, the best procedure to follow is to obtain the advice of neighboring farmers, county agricultural agents, and the state agricultural college. You will probably be told that it is better to raise a small quantity of several crops rather than a plentiful amount of a single one. Then there is always the question of feed; whether to buy it or raise it often depends on how much money is available for this purpose.

If you have read this far and are still intrigued by the thought of part-time farming, you might turn to an excellent book called "Practical Animal Husbandry," by Jack Widmer (Charles Scribner's Sons, 1949). He asserts that anyone interested in farming will be surprised at how quickly it is possible to learn to handle farming problems. The author emphasizes the importance of owning a deep freeze unit and supplies some intriguing information about sheep, hogs, rabbits, turkeys, chickens, ducks, geese, squab, guinea fowl, and beef and about meat processing. He speaks of his farm in northern California, where he has fields of hay, grain, and pasture which supply feed for his animals and a cash income from the surplus.

Many forest products, such as fuel wood, saw logs, veneer logs, posts, pulpwoods, crossties, and piling, can bring ready cash. In certain areas it is possible to grow many types of green nuts, berries, and evergreen trees. Turpentine, maple syrup, and cascara bark can find a market, and should you find yourself with an abundant supply of wild shrubs, there is a demand for them from people who have moved to suburban areas. For those who are attracted to raising bees, only a small investment is required, since bees do not require an abundance of attention.

Although most herbs are grown readily, they, too, must be studied beforehand. Many farmers start out with the six best known herbs, sweet basil, chervil, sweet marjoram, thyme, rosemary, and tarragon; then with more experience one can add the so-called mixers, chive, parsley, and summer savory. When you have become a proficient farmer and have developed a keen taste, similar to that of the gourmet, you can add to your stock anise, caraway, celery, fennel, garlic, and mint. Herbs are the ornamental touches you give to your farm. They can be grown in flower beds, rock gardens, or in special herb gardens situated right outside of the kitchen.

Fur farming is a long-term project and there is no easy route to profit. This specialized type of farming holds a great deal of attraction for physicians, however, especially in the creation of various mutations among fur-bearing animals. Cross-breeding, once begun as a scientific experiment, has grown to be one of the most profitable aspects of fur production. The quickest way to become familiar with the specialized body of knowledge is to visit successful fur farms and talk to the owners. Some states require licenses; therefore, before embarking on the raising of mink or chinchilla, it is best to write to the Department of Agriculture for a list of fur farm associations. You will then be able to learn about breeders, prices, and places to buy stock. Since the fur business is also a fashion business it is advisable to make a study of current fashion trends. At present mink is a most popular item, but one never knows when the fashion cycle will change and fickle fashion turn to another flirting pelt. Other fur-bearing animals are so plentiful, namely beaver, skunk, and muskrat, that there is little point at present in raising these animals for commercial purposes. This would be at best a rather costly bit of amusement.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Serum Cholesterol in an Office Practice. A. I. Josey. J. South Carolina M. A. 54:439-443 (Dec.) 1958 [Florence].

The author made 216 determinations of the serum cholesterol level in 59 patients seen in his private office. There were 57 men and 2 women, all in middle or later period of life. The Bloor method employing the Lietz photrometer was used, and all blood samples were obtained in the morning after a fasting period of at least 12 hours. Twenty-four of the 59 patients did not present any clinical evidence of atherosclerosis. Of these 24 patients, 11 had one or more determinations in which the serum cholesterol level was 250 mg. per 100 cc. or below and 13 had one or more determinations above 250 mg. The remaining 35 patients had definite evidence of one or more of the complications of atherosclerosis. Of these 35 patients, 17 had one or more cholesterol determinations of 250 mg. and above, and 18 had determinations below 250 mg. Eight patients with myocardial infarction fell into the group with serum cholesterol levels above 250 mg. per 100 cc., and 9 cases of infarction occurred in the group of patients with serum cholesterol levels below 250 mg.

Sixteen patients with clinical manifestations of atherosclerosis, who were chosen for their motivation and ability to cooperate, were put on maintenance therapy with a diet low in saturated and hydrogenated fats in conjunction with corn oil, and a preparation of safflower oil containing 80% linoleic acid, in doses of 15 to 30 cc. daily, was regularly prescribed for from 5 to 12 months. The total caloric intake was adjusted in each patient to obtain or maintain an optional weight. These 16 patients had serum cholesterol determinations at intervals of one month or more for a total of 5 to 10 determinations. Twelve of the 16 patients had no significant changes in serum cholesterol levels; 4 patients showed a tendency to a lowered level, but this was not consistent or persistent. The diet, therefore, failed to reduce consistently the levels of serum cholesterol in this group of 16 patients.

The level of serum cholesterol above or below 250 mg. per 100 cc. in single or serial determinations did not reflect the presence or absence of clinical complications of atherosclerosis in the 59 patients. The level of serum cholesterol found at various intervals was quite variable and erratic in presumably normal individuals and in atherosclerotic men, and because of this variability the serum cholesterol level does not appear to be of any value for the prognosis of the development of complications of atherosclerosis.

On the Bradycardic Effect of Reserpine. T. Albano and R. Motta. Minerva med. 49:3904-3909 (Oct. 17) 1958 (In Italian) [Turin, Italy].

The bradycardic effect of reserpine was studied in 38 patients with sinus tachycardia; this condition was due to mitral valvular disease in 8 patients, essential hypertension in 10, chronic cor pulmonale in 4, hyperthyroidism in 5, neurodystonia in 6, and atrial fibrillation in 5. Each patient received an initial dose of 1 mg. of reserpine per day, given intravenously for 4 to 6 days, and a maintenance dose of 0.25 mg. per day, which was continued for as long as the clinical course required it. A return to normal values was obtained within 3 to 5 days in the heart frequency of the 8 patients with mitral valvular disease; subjective symptoms disappeared. The heart action of a 21-year-old woman, who presented tachycardia both at rest and on exertion, dropped within 3 days from 144 to 70 beats per minute, and her general condition improved. Reserpine alone was sufficient to check the marked tachyarrhythmia of one patient with atrial fibrillation; this patient had derived little benefit from previous treatment with digitalis or quinidine. Reserpine was likewise beneficial in 2 of the remaining 4 patients with atrial fibrillation. The pulse rate dropped markedly in the 10 patients with essential hypertension. Good results were obtained in the 4 patients with cor pulmonale: the frequency of the heart became normal, dyspnea disappeared, and cyanosis became more attenuated. Good results were also obtained in the 5 patients with hyperthyroidism and in the 6 with neurodystonia. Side-effects occurred in 2 patients. In one patient with total arrhythmia the treatment had to be suspended because of marked subjective disturbances, which could not be checked by re-

The place of publication of the periodicals appears in brackets preceding each abstract.

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ducing the daily dose of reserpine; the other patient suffered marked asthenia, which was checked by changing the dose of 1 mg. given intravenously to 0.5 mg. given by mouth.

Familial Occurrence of Congenital Heart Disease: Report of Three Families and Review of the Literature. R. A. Carleton, W. H. Abelmann and E. W. Hancock. New England J. Med. **259**:1237-1245 (Dec. 25) 1958 [Boston].

The authors report on 3 families who were studied at the heart station of the Boston City Hospital; among the members of these families 9 with congenital heart disease were found. The first family was composed of the parents and 9 children, and 3 of the latter had congenital heart disease; the second family was composed of the parents and 5 children, and 2 of the latter had congenital heart disease; the third family was composed of 72 members, and 3 sisters and the daughter of one of these sisters had congenital heart disease. One patient in the first family, 2 persons in the second family, and the 3 sisters in the third family had a defect of the atrial septum. Six of the 9 patients with congenital heart disease underwent cardiac catherization; it was this procedure which revealed a defect of the atrial septum in the 3 sisters in the third family, thus permitting the first report of 3 cases with a defect of this type in one family diagnosed by other than clinical means. An additional 141 cases of multiple familial congenital heart disease were collected from the literature, including 4 families with more than one member with a defect of the atrial septum. Environmental gestational factors may sporadically be causative, but the findings in the patients reported on appear to conform best with a single, recessive, autosomal mode of genetic transmission.

Staphylococcal Parotitis. R. G. Petersdorf, B. R. Forsyth and D. Bernanke. New England J. Med. **259**:1250-1254 (Dec. 25) 1958 [Boston].

The authors report on 3 men and 4 women, between the ages of 50 and 85 years, with a virulent and hitherto rare form of hospital-acquired staphylococcic parotitis. With one exception, the patients were advanced in age and had severe, debilitating, chronic diseases. In 3 patients, in whom the parotitis was intimately related to a major surgical procedure (cecostomy, suprapubic prostatectomy, or cholecystectomy), the infection within the salivary gland appeared within a week of the operation. In 6 patients the parotitis occurred in the hospital, and in 1 it occurred 2 weeks after discharge from the hospital. Dehydration seemed to be an important predisposing factor and was present in 5 patients. One patient, however, had massive edema. The presence of a tracheostomy tube may have played a part in 2 patients. The clinical picture was characterized by the sudden onset of a firm, warm, erythematous, indurated swelling at the angle of the jaw and over the cheek, associated with fever, local pain, and tenderness and with a high white blood cell count (mean count, 33,000 per cubic millimeter).

Staphylococci were isolated in all patients from the pus released from the orifice of Stensen's duct and were cultured in 6 patients. The organisms were invariably resistant to penicillin, streptomycin, and the tetracyclines; some were inhibited by erythromycin and chloramphenicol; and all were sensitive to neomycin, bacitracin, nitrofurantoin, and novobiocin. Phage typing indicated the presence of an unusually resistant strain (type 80-81) in 3 patients. Five patients survived, and 2 died. Treatment was most effective when antibiotics to which the organisms were sensitive were employed. There was no relationship between the response to treatment and the nature or severity of associated disease. Dehydration and routine prophylactic use of antibiotics should be avoided, since they appear to be the most important predisposing factors in the development of staphylococcic parotitis.

Erythema Infectiosum (Megalerythema): Epidemic in West Germany. H. T. Schreus. Deutsche med. Wchnschr. **83**:2165-2167 (Dec. 5) 1958 (In German) [Stuttgart, Germany].

A large number of patients with erythema infectiosum are being seen by general practitioners and industrial physicians and in clinics in West Germany. The symptoms and the course of the disease in the individual patient show that the disease is not new. Epidemics of this skin eruption, which has been designated as erythema infectiosum, epidemic megalerythema, Ringelröteln (ring rubella), large-spotted disease, or simply fifth disease, were reported several times before in Germany. The present epidemic seems to be much more extensive than the previous ones, although exact figures of the incidence of erythema infectiosum cannot be given, since it is not a reportable disease. Another unusual aspect of this epidemic is that the disease is more frequent in women than in children. As regards the nomenclature, the author feels that the term "ring rubella" is inadvisable, because erythema infectiosum has no relation to rubella (German measles).

The disease usually begins in the face or as an enanthem in the mouth, that is, the fauces and the mucosa of the soft palate are somewhat red and occasionally may even show petechial hemorrhages. Spotty outlines on the buccal mucosa and slight redness of the tongue are also observed occasionally. At about the same time, spotty or confluent redness is observed on the cheeks. There may be complaints about itching, moderate headaches, las-

situde, and mild sore throat. Increase in temperature is slight. Extension of the eruption from the cheeks to the neck, and from there to the upper arms and wrists, sometimes sparing the elbow region, is rather rapid, as is also the extension to the lower extremities. During the early stage, the eruption resembles that of measles, except that it is somewhat more papular; it is intensely red. The small papular form of eruption usually does not persist until disappearance, but may be followed by large-surfaced, confluent areas of erythema, with relatively sharp but irregular outlines (map-like). The center may become lividly blue, and then dirty brown, whereas the rim remains red, so that at this stage the term "Ringelröteln" may seem justified. The process is not limited to the extremities, for as during the present epidemic the entire body may be involved, even to the palms of the hands and the soles of the feet.

The duration of the exanthem varies; sometimes it is subsiding on the face, while it is still in "full bloom" on the extremities. The etiology has not been completely clarified, but a virus origin is widely accepted. The prognosis is favorable, and no damaging effects on the fetus have been observed when erythema infectiosum occurred in pregnant women. The simultaneous appearance of cases in families and industries is more evident than are successive attacks resulting from contacts. This fact and the favorable prognosis indicate that isolation of patients and closing of schools and factories are unnecessary. As regards treatment, the author recommends only symptomatic therapy, since active therapy might interfere with the immunization processes that are characteristic of the exanthematic diseases.

Histoplasmosis in East Africa. P. E. C. Manson-Bahr. East African M. J. 35:625-629 (Nov.) 1958 [Nairobi].

Histoplasma capsulatum, the organism causing histoplasmosis, is found in 2 forms: (1) the mold-like saprophytic form and (2) the yeast-like parasitic phase. H. dubosii, which is the African form of the Histoplasma organism, is larger in size than H. capsulatum. Infection is caused by the mold phase, which lives in the body as the yeast phase and invades the reticuloendothelial system. Infection is from the saprophytic form in the soil, which has been contaminated by the droppings of birds and bats. The disease does not spread from man to man, but infection takes place from the inhalation or ingestion of dust. Thus, in the epidemiology of this disease enclosed spaces, such as caves, pigeon lofts, and chicken houses, where there is contaminated soil, are of great importance. There are 3 main forms of the disease: the localized form, the generalized disseminated form, and benign pulmonary histoplasmosis. After discussing these 3 forms on the basis of literature reports, the author comments on the incidence of sensitivity to histoplasmin in various regions. Surveys in Africa have shown that sensitivity rates vary from 0 to 17.8% in different parts of the continent, miners from the gold mines of Nyanza province in East Africa showing the highest incidence among miners in Africa. An interesting form of benign pulmonary histoplasmosis in South Africa is known as "cave disease." It was found in members of a speleological society, who had been exploring certain caves in the Transvaal.

Recently a patient with cave disease, the first to be described, from East Africa, came under the author's care. He contracted the disease during an exploration of the Amboni caves near Tanga in Tanganyika. There were many bats, and the floor was covered with guano. The man examined the bat guano closely for insects and ticks. Fourteen days later he started to run a fever up to 104 F (40 C) with rigors and sweats. After the first week the fever began to decline, but was still up to 101 F (38.3 C) when he was admitted to hospital about 3 weeks after the onset of symptoms. Roentgenoscopy of the lungs revealed ill-defined coarse mottlings scattered throughout both lungs. A Friedländer pneumonia or tuberculosis was considered. Later a histoplasmin skin test produced a strongly positive skin reaction to a 1/1,000 dilution. Treatment with penicillin and Chloromycetin had no effect, neither did nystatin and sulfonamides or hydroxystilbamidine and large doses of potassium iodide. The lung mottlings gradually cleared and the cough subsided, but there were still some x-ray changes in the lungs 5 months after infection.

The diagnosis of benign pulmonary histoplasmosis rests upon the history of exposure to bat guano, persistent pulmonary mottlings unlike any other condition, a strongly positive histoplasmin skin reaction, and a positive complement-fixation test. It is unusual to isolate H. capsulatum from this type of patient. Disseminated histoplasmosis should be thought of as a possibility in patients with prolonged pyrexia, with hepatosplenomegaly when leishmaniasis and brucellosis cannot be incriminated. Benign pulmonary histoplasmosis should be considered in diffuse coarse miliary mottlings of the lungs, especially where the Mantoux reaction is negative.

Urinary Tract Infection in Paralytic Poliomyelitis. H. D. Riley Jr. and V. Knight. Medicine 37:281-297 (Dec.) 1958 [Baltimore].

As the result of improved treatment of respiratory failure, there is an increasing number of survivors of paralytic poliomyelitis, in whom factors inherent in severe poliomyelitis and its treatment, including immobilization, urolithiasis, catheterization of the urinary bladder, and possibly antibac-

terial treatment, may lead to urinary tract infection. The authors studied this form of urinary infection over a 21-month period at the poliomyelitis respiratory center at Vanderbilt University Hospital, Nashville, Tenn. There were 50 patients, of whom 15 entered at the time of onset of acute poliomyelitis, while 33 were admitted 30 days or longer after onset of their disease. Two patients with acute transverse myelitis of uncertain origin have been included in this study. Thirty-five patients were over 15 years of age; 15 were younger. Twenty-six patients were males, and 24 were females. All patients were observed for periods ranging from 2 to 16 months. All but 3 patients experienced persistent respiratory insufficiency, necessitating mechanical aids to respiration. Blood pressure determinations were made at least twice daily on all patients throughout the study. Urine was collected for study weekly, or more often, from all patients regardless of evidence of urinary tract infection. Catheterization was dispensed with, and the urine specimen was collected from the midportion of the uninterrupted stream in a sterile container. The first morning specimen was not used, to avoid the overnight growth of bacteria in bladder urine.

Urinary tract infection was demonstrated in 44 of the 50 patients. It can be assumed that renal tissue damage from persistent or recurrent infections will become a factor of increasing importance in the prognosis of these patients. The disease is characterized by its indolence, frequent lack of urinary symptoms, persistence, and steady progression. Bladder catheterization and general immobilization are important influences in the development of urinary tract infection. Treatment is only slightly effective. A presumed result of frequent use of antimicrobial drugs is a high predominance of Bacillus proteus and Aerobacter aerogenes in cultures of urine. Urolithiasis was present in 21 of the 44 patients with urinary tract infection. Twenty per cent of the patients exhibited persistent diastolic hypertension, which appeared to result from some effect of poliomyelitis other than renal damage by infection.

Variations in the Course of Rheumatoid Arthritis. P. E. Brown and J. J. R. Duthie. Ann. Rheumat. Dis. **17**:359-364 (Dec.) 1958 [London].

In previous papers of this series the course of a group of patients with rheumatoid arthritis after admission to hospital was described. Changes in functional capacity and disease activity were considered for the group as a whole. The present communication is concerned with the types of course pursued by individual patients and particularly with the question of whether an appreciable number of patients showed a tendency toward permanent recovery or toward permanent disablement. Functional capacity and disease activity were determined on admission to hospital, on discharge, and at 3 subsequent assessments approximately 2 years apart. Four functional grades were distinguished. Patients with fitness for all normal activity were classified as grade 1; those with moderate restriction of function as grade 2; those with marked restriction as grade 3; and those confined to bed or chair as grade 4. Disease activity was assessed as very active, moderately active, or inactive, according to the erythrocyte sedimentation rate, the hemoglobin level, the presence of signs of inflammation in the joints, and the degree of systemic disturbance.

Studies were made on 247 patients. There seemed to be a tendency for patients to remain at approximately the same functional level for fairly long periods after treatment in hospital; 56% of the patients remained in the same functional grade at the 3 assessments after discharge, and 79% remained either in grades 1 or 2 or in grades 3 or 4. As time went on, a small percentage of patients drifted from the more favorable to the disabled groups. There was little evidence that patients in whom the disease ran the most benign course could be regarded as cured. Of those showing no disability throughout the period of observation, half continued to show signs of disease activity. Only 7% of the total number of patients retained full functional capacity and showed no signs of disease activity after discharge from the hospital. A high proportion of those who were severely disabled still showed signs of disease activity. There was no evidence that in any of these patients the disease had "burned itself out." The prognosis was most favorable in patients who had run a progressive course since the onset of symptoms and had been admitted to hospital within one year of onset.

Tophaceous Gout in a 17-Year-Old Male. K. Davison. Postgrad. M. J. **34**:651-653 (Dec.) 1958 [London].

Although tophi are present at the onset of gouty arthritis in 2% of patients, the average time between the onset of gout and the appearance of tophi is 15 to 20 years. In most of the published cases of juvenile gout, tophi were absent or did not develop till the patients were much older. The patient described was a youth of 17 years, who 18 months before admission suddenly experienced pain and swelling in the interphalangeal joints of some of his fingers. Within a few days both ankles and the metatarsophalangeal joints of both big toes were also affected. A diagnosis of acute rheumatism was made, and the patient was treated with bed rest and aspirin. The arthritis slowly subsided over a period of 2 months, but a month later both elbows became swollen and painful and remained so for a month. After an interval of 3 months the ankles,

big toes, and elbows were all affected simultaneously for a period of 3 months. Six months before admission the patient had an attack of left renal colic with hematuria. Pyelography revealed no abnormality. At about the same time he was seen by an orthopedic surgeon, who diagnosed rheumatoid arthritis. Shortly afterwards the patient noticed small nodules in his right pinna, over the right patella, and both elbows. Intermittent arthritis continued until his admission to hospital.

Examination revealed white pearly nodules in the right pinna, small subcutaneous nodules over the right patella and the right second metacarpophalangeal joint, and large yellowish nodules in both olecranon bursae, the left one having ulcerated through the skin. Effusions were present in knees and elbows, with pain and limitation of movement. The metatarsophalangeal joint of the right big toe was swollen and red. The blood urea content was 44 mg. per 100 cc., and the serum uric acid was 12.2 mg. per 100 cc. Material from the ulcerated tophus was identified as urate. The patient was treated initially with colchicine by mouth with marked symptomatic improvement. Probenecid (Benemid) was then given orally in a dose of 1 Gm. twice daily, together with a high-fluid intake and a low-purine diet. This treatment was continued, and, apart from a transient recurrence of arthritis, the patient remained symptom-free.

Juvenile gout often differs from adult gout in the absence of classical podagra and the frequent occurrence of polyarthritis. This led to diagnostic difficulty in this patient, but at the time of his admission to hospital the presence of multiple gouty tophi, together with the recurrent acute peripheral arthritis, enabled a clinical diagnosis of gout to be made, which was confirmed by the high serum uric acid level. No family history of arthritis was obtained, and the serum uric acid levels of the available relatives were all within normal limits of 4 to 6 mg. per 100 cc.

Assessment of the Relative Importance of the Allergic, Infective and Psychological Factors in Asthma. D. A. Williams, E. Lewis-Faning, L. Rees and others. Acta allergol. **12**:376-395 (no. 6) 1958 (In English) [Copenhagen].

The authors report on 487 consecutive patients with asthma, who attended the asthma clinic of St. David's Hospital in Cardiff, Wales, between 1951 and 1954. There were 274 male and 213 female patients; 248 were children, and 239 were adults. Boys predominated among the children, and women among the adults. Analysis of the causes of asthma in these patients revealed that an infective factor was present in 88%, a psychological factor in 70%, and an allergic factor in 64%. All three factors played a part in the precipitation of asthma in 38%; the infective and psychological factors only played a part in 23%, the allergic and infective factors in 15%, and the allergic and psychological factors in 7%. The infective factor was the only factor causing asthma in 11%, the allergy factor was the sole cause in 3.3%, and the psychological factor was the only cause in 1.2%. The dominant precipitating causes of asthma were the allergic factor in 29%, the infective factor in 41%, and the psychological factor in 30%. Analysis of these causes, as found among the different age groups, suggested that in children up to 5 years of age the psychological factor was the most frequent, and in the group over 45 years of age the infective factor was by far the most important precipitating cause. Supportive evidence of the likelihood of these general observations being correct is given.

SURGERY

Congenital Aortic Stenosis: Clinical and Hemodynamic Findings, Surgical Technic, and Results of Operation. A. G. Morrow, E. H. Sharp and E. Braunwald. Circulation **18**:1091-1104 (Dec.) 1958 [New York].

The authors report on 20 male and 10 female patients, between the ages of 4 and 39 years, with congenital aortic stenosis confirmed by the demonstration of a systolic pressure gradient between the left ventricle and a systemic artery. Of the 30 patients, 13 had valvular aortic stenosis, 8 had subvalvular stenosis, and in the remaining 9 patients the obstruction had not been localized. Seven of the 13 patients had anginal pain, 3 had a history of syncopal attacks, and 12 had dyspnea. Only one patient was entirely asymptomatic. Of the 8 patients with subvalvular stenosis, 4 had anginal pain, 2 had histories of syncope, and 6 had dyspnea. Two of the 8 patients were entirely asymptomatic. Every patient had a harsh systolic murmur and a thrill at the base of the heart. A high-pitched, decrescendo diastolic murmur along the left sternal border was also present in 4 of the 13 patients with valvular stenosis and in 4 of the 8 patients with subvalvular stenosis. The second heart sound in the aortic area was diminished in 8 of the 13 patients and in 3 of the 8 patients. Fluoroscopic and roentgenographic examinations of the heart revealed some degree of left ventricular enlargement in all but 3 of the 30 patients. Poststenotic dilatation of the aorta was a prominent feature in almost every patient. Angiocardiography was carried out in 11 patients and always revealed a thickened left ventricular wall and a small left ventricular cavity. Left heart catherization was performed by the transbronchial route in 19 patients. In the other 11 patients, particularly young children, left ventricular pressures were obtained by means of direct puncture of this chamber through the left side of the anterior chest wall. The aortic valve gradients,

i. e., the differences between simultaneous peak systolic pressures in the left ventricle and the aorta or a peripheral artery, ranged from 15 to 172 mm. Hg. and averaged 82 mm. Hg. Right heart catherizations were carried out in 28 of the 30 patients; findings suggested encroachment by the enlarged left ventricle on the interventricular septum and right ventricular outflow tract.

Eighteen of the 30 patients were operated on at the surgical clinic of the National Heart Institute in Bethesda, Md. A closed transaortic or transventricular operation was performed on the first 4 patients; surgical intervention under direct vision with the aid of general hypothermia was carried out in the next 11 patients; and the last 3 patients were operated on with the aid of extracorporeal circulation and elective cardiac arrest with the patients at normal temperature. Thus, 14 of the 18 patients were operated on with direct exposure of the aortic valve. Three of the 18 patients died, one of irreversible ventricular fibrillation occurring after the period of inflow occlusion, one of septicemia produced by Pseudomonas organisms 5 weeks postoperatively, and one 10 days postoperatively of massive intrathoracic hemorrhage after the administration of heparin and bishydroxycoumarin (Dicumarol) given in the treatment of femoral thrombophlebitis. The 15 surviving patients are free of cardiovascular symptoms, but despite these gratifying clinical results, postoperative hemodynamic studies in all but 5 indicate that some degree of residual stenosis exists.

Ten years ago congenital aortic stenosis was generally considered to be uncommon and seldom to carry a grave prognosis. The severity of obstruction of left ventricular outflow could not be directly assessed, and suitable surgical procedures for its correction were not available. The changing concepts in respect to this malformation are reflected in these 30 patients. The lesion was found to be relatively common and frequently serious. The severity and site of obstruction could be precisely evaluated, and a physiological basis was provided for the selection of patients for operation providing direct exposure of the aortic valve.

Diagnosis and Treatment of Peripheral Round Infiltrates of the Lung. I. Andersen and B. Clausen. Acta. chir. scandinav. **115**:422-426 (no. 6) 1958 (In English) [Stockholm].

The authors report on 52 patients with peripheral round infiltrates of the lung ("coin lesions"), in whom no more than a tentative clinical diagnosis was made and in whom the correct diagnosis was secured by exploratory thoracotomy. Of the 52 patients, 37 were men and 15 were women; 15 (6 women and 9 men) were less than 40 years old, and 37 (9 women and 28 men) were over 40 years of age. Thoracotomy revealed primary or secondary carcinoma in 3 patients (20%), aged less than 40 years, and in 25 patients (69%), over 40 years of age. Tuberculoma was found on surgical intervention in 8 patients (53%), aged less than 40 years, and in 5 patients (14%), over 40 years of age. Of the 52 patients, 17 underwent pneumonectomy; 17, lobectomy; 13, segmental resection; and 5, removal of pleural cysts, hamartoma, and meningocele. There were no operative deaths.

Because of the high incidence of malignant lesions in this series of patients with asymptomatic peripheral round infiltrates of the lung, prompt active surgical treatment is justified. From the form, size, and solidity of the tumor as visualized in plain chest roentgenograms and tomograms, nothing can be deduced except that the hamartomas are perhaps of less regular circular shape than the carcinomas and tuberculomas. The presence of calcification may be suggestive of tuberculoma or hamartoma but does not rule out a diagnosis of cancer. Degeneration may be seen in tuberculoma, in inflammatory processes, and in carcinoma. In most patients bronchography, bronchoscopy, and the study of aspirated bronchial secretion did not provide additional information. Because of the difficulties observed in the preoperative differential diagnosis, extensive use of exploratory thoracotomy is recommended, in the course of which frozen sections of biopsy specimens are subjected to microscopic examination. On the basis of the operative and microscopic findings, the authors determine the type and extent of the operation to be performed.

Clinical Application of a New Flexible Knitted Dacron Arterial Substitute. M. E. DeBakey, D. A. Cooley, E. S. Crawford and G. C. Morris Jr. Am. Surgeon **24**:862-869 (Dec.) 1958 [Baltimore].

Since early in 1957 the authors have employed seamless knitted, cleansed but chemically untreated Dacron tubes, in different sizes and in the form of bifurcations as well as multibranch tubes, in the treatment of a wide variety of aortic and arterial diseases, such as occlusive disease of the abdominal aorta and iliac arteries and extensive fusiform aneurysm of the descending thoracic aorta. Analysis of this experience, which now includes a total of 737 cases, reveals results that are, in general, most satisfactory. Although insufficient time has elapsed to provide long-term evaluation of the functional efficacy of these grafts, follow-up observations for periods ranging from 1 to 1½ years have been most gratifying and within this period of time have revealed no failures which could be attributable to the graft. An aortogram made one year after surgical intervention in a patient with extensive arteriosclerotic aneurysm of the abdominal aorta involving the bifurcation and common iliac arteries showed excellent functioning of the bifurcation

Dacron graft used to replace the excised portion with the aortic aneurysm. An aortogram made 14 months after operation in another patient showed restoration of circulation in the right lower extremity by means of a bypass Dacron graft attached by end-to-side anastomoses to the common femoral artery above and to the popliteal artery below.

Moreover, a comparison of these results with those obtained by the authors in their previous experience with other types of synthetic vascular replacements and with homografts indicates the Dacron graft to be superior in all respects. Particularly noteworthy is the fact that the incidence of failure attributable to the graft was significantly less in the Dacron series than in other synthetic grafts. An important factor contributing to the reduction in deaths in the more recent Dacron series is improvement in surgical management resulting from increased experience. The fact remains, however, that the mortality in the Dacron series is significantly lower than in the other series, and this fact, along with the distinctly higher incidence of over-all successful results, provides good evidence of the clinical value and efficacy of the new arterial substitute.

Surgical Complications in a Community Hospital with Particular Reference to Wound Infections. P. J. Guthorn, H. A. Kazmann and Chang You Wu. J. M. Soc. New Jersey **55**:650-655 (Dec.) 1958 [Trenton].

The study was begun in January, 1957, at the Monmouth Memorial Hospital in Long Branch, N. J. It was undertaken as part of a surgical residency program. On the ward service, where supervision was possible, an effort was made to search for all complications. Infections on the private service were studied with the cooperation of the attending staff. Two forms were used. One was a Report of Surgical Complications to be filled out weekly on each ward or unit. The responsible house officer checked in the appropriate column. The second was the Wound Infection Report, filled out by the house officer (or, in private cases, by the attending surgeon) and forwarded when the infection had run its course. On the ward service 264 operations were performed, with 15 surgical deaths; on the private service 1,895 operations, with 29 operative deaths. On the ward service a total of 130 complications occurred in 54 patients; forty complications occurred in the 15 ward patients who died within 30 days of operation, and 42 complications occurred in the 29 private patients who died after operation, showing that there is a tendency for complications to be multiple.

The morbidity and mortality on the ward service were higher than on the private service. Factors responsible for the higher incidence of complications on the ward are the greater age, the substantial proportion of patients who are malnourished, and the tendency to seek care late in the course of the disease. Since malnourishment and undernourishment are common among ward patients, a longer time was needed in elective surgery cases to correct nutritional, blood volume, and other disturbances. The tendency to seek medical care late was also evident in the patients admitted, almost moribund, with long-standing intestinal obstruction or chronic blood loss.

A total of 49 wound infections occurred, 16 in the 264 operations on ward patients and 33 in the 1,895 operations on private patients. Frequently the period of clinical quiescence was 10 to 12 days, and in 2 patients 21 and 24 days respectively. The principal offending organism was the hemolytic Staphylococcus pyogenes var. aureus. A total of 69 purulent infections were studied bacteriologically. All were mixed infections except for a few of the face and neck. The hemolytic Staph. aureus was present in 45 of these and the nonhemolytic Staph. aureus in 32. In smaller numbers the following organisms were found: Pseudomonas aeruginosa, Proteus vulgaris, Bacillus subtilis, Escherichia coli, nonhemolytic Staphylococcus albus, diphtheroids, Clostridium organisms, and hemolytic and nonhemolytic streptococci.

There were many gaps in the bacteriological study; for instance, phage typing either was not available or was not done in sufficient numbers to demonstrate a connection between the organisms encountered in the hospital and those in the wound infections. There was evidence that the incidence of wound infections appears to be increasing, and that wound infections tend to occur as small epidemics. There was a higher incidence of antibiotic resistance in the hospital infections, although the flora of both in-hospital and out-of-hospital infections are similar.

Primary Adenocarcinoma of the Appendix: Report of 16 Cases. Acta chir. scandinav. **115**:447-456 (no. 6) 1958 (In English) [Stockholm].

The authors report on 9 women and 7 men with primary adenocarcinoma of the appendix. Thirteen of the 16 patients were over 50 years of age, 1 was 48 years old, and 2 were less than 40 years of age. The cases of these patients, who were treated at various Danish hospitals, were recorded at the Danish Cancer Registry in Copenhagen between 1943 and 1956. Most of the patients had clinical manifestations of appendicitis. Appendectomy was performed on 7 patients. Of these, 3 are still alive, without signs of recurrence, 2, 4, and 10 years after the surgical intervention. One patient died of peritonitis one week after the operation, and the remaining 3 died of recurrence 9 months, 2 years, and 3 years after the operation. Four patients were subjected to appendectomy followed by right-sided

hemicolectomy after the lapse of 5, 19, 53, and 193 days. Three of these are still alive, without signs of recurrence, 21 months, 2 years, and 4½ years after the first admission. The fourth patient, who underwent hemicolectomy 6 months after the appendectomy at a time when cutaneous metastases in the operative scar had occurred and there was macroscopically visible recurrence at the site of the appendix, died of recurrence 12 months later. Of the remaining 5 patients, 2 died in the hospital after palliative surgical measures for ileus; 3 were not operated on, 2 of them being admitted in hopeless condition and dying within a few days and 1 dying of an abdominal tumor and ascites within 2 months after admission. In all the patients, the diagnosis of adenocarcinoma of the appendix was made only at operation or autopsy. Histologically the tumors showed the same structure as cancers of the colon.

Adenocarcinoma of the colonic type is the rarest and most malignant form of carcinoma of the appendix. The diagnosis cannot be made preoperatively but is established often as a surprise, by microscopic examination. Appendectomy can be regarded as adequate treatment only when the lesion is confined to the mucosa and is of peripheral localization; in all other cases, right-sided hemicolectomy is indicated. Recovery from malignant mucocele of the appendix may be achieved by appendectomy, provided that rupture of the appendix has not given rise to peritoneal pseudomyxoma. If this has occurred, as much as possible of the gelatinous material must be removed; if the cecum shows involvement, hemicolectomy must be performed. In the presence of a carcinoid tumor, which occurs about 10 times as frequently as carcinoma, appendectomy is sufficient.

Indications for Open Heart Surgery Using Temporary Cardiopulmonary Bypass. D. A. Cooley. J. Louisiana M. Soc. **110**:407-410 (Dec.) 1958 [New Orleans].

Cooley reviews observations on 465 patients who, during the past 2½ years, were operated on with the aid of a pump oxygenator which permitted open cardiotomy during temporary cardiopulmonary bypass. Among these patients, who were treated at several hospitals in Houston, Texas, there were 392 with congenital and 73 with acquired lesions. The over-all mortality among the 164 patients operated on for ventricular septal defects was 18%. Age was an important factor in survival, the operative mortality being 40% among patients less than 2 years old and 7% among 100 patients ranging in age from 2 to 15 years. Since no deaths occurred in patients with normal or moderately elevated pulmonary arterial pressure, the author feels that almost all ventricular septal defects should be repaired.

Of the 123 patients with atrial septal defects, 90 had the ostium secundum type. The 6 deaths in this group concerned patients more than 25 years old and usually with advanced cardiopulmonary disease. The majority of patients less than 25 years old should be operated on if a significant left-to-right intracardiac shunt is present. Twenty patients with ostium primum defects were operated on, with 3 deaths. Seven deaths occurred in the 13 patients with canalis atrioventricularis communis. This complicated anomaly may be virtually incorrectible, but in many instances a satisfactory repair may be obtained.

Twenty-nine patients were operated on for the tetralogy of Fallot. In the acyanotic or minimally cyanosed patient with the tetralogy of Fallot, the results were comparable to the results in isolated ventricular septal defect. Among patients exhibiting severe cyanosis and diminutive pulmonary artery, the operative mortality was 40%. The author says that, in very small infants in critical condition from cyanotic spells, the anastomotic procedures of Blalock and Potts offer palliation. Risk of operation is low in congenital aortic and subaortic stenosis, 20 patients with this defect being operated on without a single death. Among 22 patients operated on for pulmonic valvular and infundibular stenosis, one died. Excellent results are obtained with open heart surgery in these lesions. Of 10 patients operated on for total anomaly of pulmonary venous drainage, 7 survived. The 3 deaths occurred in patients with complicating features making any form of surgical attack extremely risky. Complete repair was achieved in 3 patients with aorticopulmonary septal defect.

In 6 patients with transposition of the great vessels, surgical correction with use of the pump oxygenator was not successful. Poor results were obtained also in 15 patients with miscellaneous congenital defects, such as mitral atresia, single ventricle, tricuspid atresia, truncus arteriosus, and Ebstein's disease.

Those with acquired lesions who underwent open heart surgery included 24 with calcific aortic stenosis. The results of operation on these patients were encouraging. Regarding mitral stenosis, the author says that division of the commissures under direct vision permits accurate repair of the mitral stenosis and control of thrombi and embolism from the left atrium. This technique was used in 10 patients, all of whom had previously undergone closed commissurotomy. The procedure, which at present is reserved only for the recurrent lesions, may later be used for primary operations. All 4 patients subjected to operation for ventricular aneurysm after myocardial infarction survived with good functional results. Treatment was successful in 3 patients with cardiac myxoma. Good results were obtained also in 3 patients with stab wounds or blunt injuries of the heart.

Abdominal Repair of Hiatal Hernia: A Study of 138 Cases. E. S. Crawford and M. E. DeBakey. Am. Surgeon **24**:889-895 (Dec.) 1958 [Baltimore].

The authors report on 138 patients with hiatal hernia who were treated surgically at the Jefferson Davis, Methodist, and Veterans Administration Hospitals in Houston, Texas, between 1951 and 1958. There were 72 men and 66 women, but, if the patients treated at the Veterans Administration Hospital are excluded, there were more women than men. The ages of the patients ranged from 32 to 85 years, with more than 33% being over 60 years of age. The transthoracic approach was used in 24 patients and the abdominal in 114. The transthoracic route was used in most of the early cases, but during the past 4 years this approach has been employed only in patients with other thoracic lesions. The increasing preference for repair of the hiatal hernia by the abdominal route has been caused by frequent association of the hiatal hernia with other lesions, such as cholelithiasis, duodenal ulcer, and leiomyoma of the intestine. In patients with such associated lesions, the latter may be surgically treated at the same time that the hernia is repaired if the abdominal route is employed. There were 57 abdominal lesions associated with hiatal hernia in the 114 patients subjected to abdominal repair; in addition, appendectomy was performed on 47 patients, gastrostomy and digital esophageal dilatation on 9, and bilateral lumbar sympathectomy on 1.

The technique employed for the abdominal repair of the hernia included an upper abdominal midline incision and exposure of the hiatal region by retraction of the liver medially and the stomach downward. Retraction of the stomach downward reduced the hernia and permitted exposure of the hiatus through an incision in the peritoneum between the esophagogastric junction and the diaphragm. This exposure was completed by encircling the esophagus with umbilical tape for traction and dissecting the retroperitoneal fibrofatty tissue from the lateral margins of the hiatus. The hiatus was reduced to normal size by approximating the lateral margins behind the esophagus and suturing the esophagogastric junction to the under surface of the new esophageal opening.

Two of the 138 patients died, and these 2 deaths occurred among the patients treated by transthoracic repair; one was due to myocardial infarction, and the other to disruption of the diaphragmatic incision. Hiatal hernias recurred in 2 patients subjected to thoracic repair and in 4 subjected to abdominal repair. Symptoms, such as burning pain, vomiting, regurgitation, hematemesis, melena, dysphagia, belching, and nausea, were relieved in all patients who had successful abdominal repair; however, of 3 patients subjected to thoracic repair, 2 later required cholecystectomy and 1 required gastrectomy for relief of symptoms. The effectiveness of the technique employed in the abdominal repair of hiatal hernias was evident in the extremely low incidence of recurrence (3.5%) and the safety with which it was combined with other abdominal procedures.

Adenomas of the Adrenal Cortex. M. M. Desyatov and M. G. Trachtenberg. Khirurgiya **34**:35-41 (no. 10) 1958 (In Russian) [Moscow].

Modern methods of examining patients with endocrine diseases, such as suprarenopneumography, determination of urinary 17-ketosteroid concentration, and the cortisone test, facilitate the diagnosis of adrenal cortical adenoma. The authors present 20 case reports of patients with the Itsenko-Cushing syndrome. The patients were subjected to lumbotomy and excision of the tumor. The operation was carried out with the patient under oxygen–ether or spinal anesthesia. To prevent suprarenal insufficiency, the patients were treated preoperatively with preparations derived from the adrenal cortex—corticotropin (ACTH) and desoxycorticosterone acetate. Cortin and cortisone were given during the postoperative period. Two patients died. A stable positive effect was observed in the rest of the patients, and the clinical symptoms of this disease gradually disappeared. Women treated by this method began to menstruate again. Excessive hair on the face, body, and extremities disappeared. These women reduced in weight, their arterial blood pressure became stabilized, and they experienced no headaches or general weakness.

Contributions to the Pathological Anatomy of Thrombosis and Embolism. A. I. Strukov and N. N. Vasilieva. Khirurgiya **34**:86-96 (no. 10) 1958 (In Russian) [Moscow].

The authors present a statistical analysis of thrombosis and embolism for 20 years (1938-1957), based on data of the department of pathological anatomy of the Sechenov Medical Institute in Moscow. Fourteen thousand eight hundred fifty-three autopsies were performed during that period, and 128 embolisms of the pulmonary artery (0.86%) were recorded. The incidence of this complication rose in the years between 1940 and 1954 from 0.91 to 3.92% but was totally absent during the war period (1942-1945). This confirms the observations of foreign authors. The rise in the incidence of thromboembolism of the pulmonary artery coincides with the increase in the percentage of tumors and diseases of the cardiovascular system as the cause of death. The distribution of thrombosis and embolism among different nosological forms demonstrated that the first place is occupied by diseases of the cardiovascular system, constituting 56% of the thromboses and 37% of all the thromboembol-

isms of the pulmonary artery. The incidence of thrombosis and embolism among patients with tumors of various localizations appeared to be lower than among those with diseases of the cardiovascular system. The absolute number of thromboses and embolisms in the group of tumors is still high (26% of all thromboses, 38% of all thromboembolisms of the pulmonary artery). The veins of the lower extremities, the right heart (especially the right auricular appendage), and the veins of the small pelvis constitute the source of thromboembolism of the pulmonary artery. The authors recommend the use of anticoagulants in the treatment and in the prophylaxis of thromboembolism of the pulmonary artery.

Modern Therapy of Blood Coagulation Disturbances. D. M. Grozdova and V. A. Agranenko. Khirurgiya **34**:101-108 (no. 10) 1958 (In Russian) [Moscow].

The use of anticoagulants in surgical clinics has a pronounced therapeutic effect in the acute and subacute stages of thrombosis and thrombophlebitis. In the treatment of acute thrombosis and of thrombophlebitis, the most rational method is the administration of preparations of the heparin and coumarin groups. The most effective method of treatment, which makes possible prevention of recurrence of the disease and of various complications, is the surgical treatment of thrombophlebitis. Anticoagulant therapy is indicated after surgical treatment of thrombophlebitic splenomegaly, portal hypertension, and diseases in which splenectomy or vascular anastomosis is required. This therapy decreases the danger of postoperative thrombosis. Intravenous injection of heparin is most effective in acute stages of thrombosis. Intramuscular injections of heparin at intervals of 6 to 12 hours prolong its action. Prolonged anticoagulant therapy is indicated in the recurrent form of thrombophlebitis of the extremities and in patients with a history of myocardial or pulmonary infarction. This treatment is conducted under control of the prothrombin concentration (65-80%). The authors' observations of such prolonged therapy (from 2 months to 2 years) showed the absence of recurrence of the disease or of untoward side-effects due to the administration of the anticoagulant drug.

Hematological Changes After Total Gastrectomy. W Kothe. Beitr. klin. Chir. **197**:184-191 (no. 2) 1958 (In German) [Munich].

Total gastrectomy was performed on 59 of 1,083 patients with carcinoma of the stomach at the Karl Marx University of Leipzig between 1945 and 1956. The 40 patients who have survived from 1 to more than 4 years have all required special care, because, with total loss of the stomach, metabolic as well as hematological changes can be expected. Literature reports on blood changes after total gastrectomy are mentioned, and the author describes studies of iron metabolism, by means of iron tolerance tests, on 21 patients on whom gastrectomy had been performed up to 4½ years previously. There was evidence that iron resorption becomes impaired after total gastrectomy.

Total loss of the stomach generally produces hematological changes, which progress in phases from hypochromic anemia to megalocytic anemia of half-pernicious character to true pernicious anemia. The time of appearance of each phase differs, as it is not entirely dependent on the duration of absence of the stomach. After a patient has survived total gastrectomy for 3 years, the blood picture (the peripheral and the bone marrow punctate) should be examined at intervals of 3 months, because the author found that the development of pernicious anemia may take place within a few months.

Surgico-Angiological Problems in Diabetes Mellitus. G. Meyer-Burgdorff and E. Kricke. Beitr. klin. Chir. **197**:139-151 (no. 2) 1958 (In German) [Munich].

The authors are concerned with whether the vascular lesions of diabetes mellitus represent a special form of angiological disease. The question is raised whether the metabolic disorder or the treatment with insulin is the decisive factor in the pathogenesis. Although specific diabetic changes in the structure of the vascular walls have not been demonstrated, numerous factors have been cited to show that "diabetic angiopathy" does represent a special form. It is characterized by premature sclerosis, particularly of the terminal vessels, and the resulting stasis leads to secondary changes in the conveyor arteries. The capillary damage, as a rule, appears only after the diabetic disorder has existed for from 5 to 15 years, but sometimes very severe forms of vascular disease are observed in young diabetic patients. Although some investigators include only nephropathy (Kimmelstiel-Wilson disease) and retinopathy in the concept of "diabetic angiopathy," others also include gangrene of the extremities, and this last form is of particular interest to the surgeon. The authors cite figures to demonstrate the high incidence of gangrene of the extremities in diabetics.

In discussing the influence of insulin on the blood perfusion of various tissues, the work of several investigators on this problem and that of one of the authors are cited. The observed increased blood perfusion of the muscles of diabetics indicates increased capillarization, and the blood perfusion of these capillaries is further increased by insulin. The increased blood perfusion of the muscles apparently is at the expense of the blood perfusion of

the skin. Deficient circulation in the skin, however, is likely to cause necrosis and gangrene, and since insulin acts chiefly on the muscles, it may be regarded as indirectly responsible for gangrene, rather than as having a retarding effect on the development of that condition.

Since exclusion of the sympathetic system promotes the blood perfusion of the skin, the authors advocate sympathectomy for the prevention of diabetic gangrene. They report their observation on 61 diabetic patients with vascular complications in the extremities. Twenty-two of 42 patients who had received conservative treatment and 10 of 19 who had been subjected to sympathetectomy required subsequent amputation, that is, the same percentage in both groups. However, taking into account the level of the amputation, it was found that, whereas 80% of the amputations after conservative treatment were extensive, only 33% of those after sympathectomy were extensive. This indicates that sympathectomy in diabetics during the stage of necrosis shifts the level of the amputation in the distal direction. The authors advocate sympathectomy as a prophylactic measure against gangrene of the extremities in diabetic patients.

Multiple Hemangiomas of the Jejunum as a Cause of Massive Gastrointestinal Bleeding. A. L. Evans, O. S. Cofer and H. H. Gregory. J. M. A. Georgia **47**:600-603 (Dec.) 1958 [Atlanta].

The authors cite figures from the literature, which prove the extreme rarity of hemangiomas of the small intestine, and present the history of a male patient who had had no intestinal bleeding until he was 61 years old. When hospitalized at age 63, in July, 1957, this patient complained of epigastric discomfort and bleeding from the rectum. He stated that approximately 2 years prior to admission, while at stool, he passed large amounts of bright red blood through the rectum. He became so weak that he fainted. After that time, at about 2-month intervals, he had other similar episodes. He had been thoroughly examined by several physicians and at 2 university clinics and was told that all x-ray, sigmoidoscopic, and fecal examinations were negative. He was advised to have an exploratory laparotomy but refused. Eight months prior to admission he began to have constant epigastric pain of a burning nature, which radiated under his ribs and sternum. He was treated for this with a bland diet and antacids with little relief. The pain had become progressively worse and was constant day and night. It had no relation to meals but was aggravated by deep breathing or stooping over. After thorough examination the patient was told that the cause of bleeding could not be located and was advised to have an exploratory laparotomy. On the 5th day after admission he had severe melena and consented to surgical exploration.

The small intestine was explored first, and at the ileocecal area and along the ileum small bluish nodules were noted. As the jejunum was approached, these became more numerous. The proximal jejunum was studded with numerous bluish nodules, varying in size from 3 to 16 mm. (matchhead to size of a dime). Examination of the stomach, liver, colon, and other abdominal viscera failed to reveal further tumors. It was decided to resect only the proximal part of the jejunum in the hope that the bleeding had arisen from the larger tumors; the proximal 90 cm. of the jejunum, beginning 3 cm. distal to the ligament of Treitz, was resected. An end-to-end jejunojejunostomy was done. The postoperative course was uneventful. Examination of the specimen disclosed that the background of the bluish nodules was that of cavernous hemangiomas in the submucosa. There was no evidence of malignancy. The patient experienced further hemorrhages, requiring blood replacement after the operation. Since the entire small intestine cannot be removed, it was hoped that another look might uncover the chief area of bleeding or that multiple mural excisions could be considered.

The commonest presenting symptom of multiple hemangiomas of the small intestine is bleeding from the rectum. A few cases have been reported in which there was intestinal obstruction or intussusception, and occasionally inflammation of the tumor simulated appendicitis. In some cases, these intestinal hemangiomas cause only vague abdominal symptoms. Large hemangiomas may be diagnosed preoperatively by characteristic phleboliths in the roentgenogram. The diagnosis is usually made by exploratory laparotomy or at autopsy. Repeated melena with unexplained anemia or numerous hemangiomas of the skin should arouse suspicion of intestinal hemangioma. The patient presented had a hemangioma on the lip. Hemangiomas should be considered before doing a "blind" gastric resection. The treatment is surgical; results are excellent in single lesions, poorer in multiple lesions.

Cause of Death in Surgery of the Newborn: Emphasis on Prevention of Aspiration. R. Spencer. J. Louisiana M. Soc. **110**:418-422 (Dec.) 1958 [New Orleans].

This report is concerned with 74 infants, less than 1 month of age, who in the course of the last 3 years were observed on the pediatric surgery service of the Charity Hospital of Louisiana in New Orleans. Twenty-eight of these 74 infants died. This study includes all the infants who were operated on, or whose condition was diagnosed as being a surgical one, on or before the 30th day of postnatal life. Twenty-one of 37 infants with early congenital anomalies died. Their average age at

operation was 4 days. More than half of the deaths were due to pulmonary complications—atelectasis and pneumonitis. The anomalies in this group were congenital obstructive lesions of the alimentary tract, perforation of the stomach as a result of an abnormality in development, omphalocele, Siamese twins, and multicystic kidney. There were no deaths among the 17 patients with late congenital anomalies, which included pyloric stenosis, incarcerated inguinal hernia, and Hirschsprung's disease. The average age of these infants was 23 days.

All 6 infants with noncongenital emergencies early in the neonatal period died. This group included 2 infants with paralytic ileus due to sepsis, a 9-day-old, 900-Gm. (2-lb.) baby with a bleeding gastric ulcer, and 3 1,400-Gm. (3-lb.) infants with a condition labeled constipation-dehydration. These dehydrated patients apparently died of intestinal obstruction produced by plugs of inspissated milk curds. At autopsy there was increased fibrosis in the pancreas of one of these patients. All 3 infants treated for trauma survived. The only death among 11 infants with miscellaneous conditions concerned a 3-week-old baby with a cystic hygroma of the axilla, who had diarrhea, then pneumonia, and finally died of viral hepatitis and septicemia due to Escherichia coli 13 days after operation.

The deaths due to multiple congenital anomalies were mostly unavoidable, but the largest group of deaths, those due to pulmonary complications, should be preventable. The most important factor in prevention of death from aspiration is early diagnosis and treatment of congenital obstructive lesions of the alimentary tract. Any infant who is difficult to resuscitate at birth or who has intermittent cyanosis and excessive mucus should be suspected of having atresia of the esophagus with tracheoesophageal fistula until the diagnosis has been excluded by passing a catheter through the esophagus and into the stomach. Every newborn infant who vomits, particularly if the vomitus contains bile, should be subjected to roentgenoscopy of the abdomen to rule out congenital intestinal obstruction. If tracheoesophageal fistula with esophageal atresia is suspected because of inability to insert a nasogastric tube, the diagnosis should be confirmed by fluoroscopy.

Once the diagnosis of intestinal obstruction is made, x-ray studies with contrast material are contraindicated. The infant should be placed on his abdomen, and decompression of the gastrointestinal tract should be undertaken. In these small patients the ordinary urethral catheter is superior to the Levin tube. Gravity drainage and intermittent aspiration of the catheter with a syringe are preferable to strong constant suction. Preoperative decompression of the gastrointestinal tract cannot be overemphasized. Frequent suction of the nasopharynx is almost as important in intestinal obstruction as in tracheoesophageal fistula. Newborn infants have poor cough reflexes and many aspirate the increased secretions resulting from the irritation of the nasogastric tube. Additional preoperative measures for both tracheoesophageal fistula and intestinal obstruction include minimal but adequate hydration, transfusion if necessary, antibiotics, and administration of an adequate drying agent before induction of anesthesia. The smaller the infant, the more important is this last measure.

Postoperatively, all these patients require an atmosphere of high humidity, suction of the nasopharynx, and the prone position. Even with the most expert nursing care, these tiny patients, who have poor gag and cough reflexes, will often aspirate secretions—usually with disastrous results. For this reason, gastrostomy is recommended in congenital intestinal obstruction.

NEUROLOGY & PSYCHIATRY

Horse Serum Neuropathy. A. A. Marinacci. Bull. Los Angeles Neurol. Soc. **23**:149-159 (Dec.) 1958 [Los Angeles].

This study is concerned with electromyographic studies on 115 patients who had muscular paralysis in the region of the shoulder girdle and arms. These patients had received serum therapy in the form of tetanus antitoxin for lacerations or deep wounds. Electromyographic studies demonstrated that this horse serum plexitis can be misinterpreted and that other disease entities have been falsely incriminated. This results because the disorder has a latent period of from 6 to 12 days after the injection of antitoxin. When the paralysis appears a week or 2 after the injection, the serum therapy has usually been forgotten. Another important fact is that the paralysis usually is focal and may involve either a group of muscles supplied by a single peripheral nerve or the group of muscular structures innervated from the fifth cervical nerve root or an isolated peripheral nerve such as the axillary nerve.

Electromyography proved valuable not only in revealing the true nature of this neuropathy but also in differentiating it from other diseases. Electromyographic studies revealed more widespread involvement than did the clinical signs. It was found that the roots and trunks of the brachial plexus are rarely involved and that its cords are only occasionally affected. The damage is largely limited to the proximal peripheral nerves which have their immediate origin from the roots of the brachial plexus, such as the dorsal scapular and long thoracic nerve of Bell, from the trunks, such as the subclavian and suprascapular nerves, or from the cords, such as the medial and lateral anterior thoracic, subscapular, thoracodorsal, axillary, and musculocutaneous nerves. The terminal branches

of the cervical plexus are also affected, while the radial, median, and ulnar nerves are rarely involved directly. Occasionally involvement of either the radial, median, or ulnar nerves may be seen. However, the involvement in these nerves is due to pressure on the nerve while the patient is in bed and not due directly to the horse serum itself. The most commonly affected nerve is the axillary, next the suprascapular, then the musculocutaneous, the cervical plexus, and the long thoracic nerve, and finally the dorsal scapular.

This neuropathy resembles several other conditions, particularly anterior poliomyelitis, cervical cord tumor, amyotrophic lateral sclerosis, cervical cord trauma, cervical nerve root compression, a lesion of the upper trunk of the brachial plexus, shoulder-hand syndrome, and finally cerebral vascular accident. The peripheral effects of this disease entity are further substantiated by its favorable prognosis for complete recovery from the paralysis. It is the author's opinion that this disease should be designated as a horse serum neuropathy rather than as a horse serum "plexitis," because the plexus per se is not involved in the majority of instances. Finally, because horse serum neuropathy stems from trauma, the electromyogram makes clear its relationship to an industrial as well as a medicolegal prognosis, especially when the patients are observed for as long as 3 years.

Routine Blood Control on Permanent Treatment with Mesantoin and Dimedion. E. Kjøboe and E. Kroman. Nord. med. **60**:1599-1602 (Nov. 6) 1958 (In Danish) [Stockholm].

In 59 patients treated with Dimedion and in 110 treated with Mesantoin, the treatment was usually started during hospitalization and continued after the patient was made ambulant. Leukocyte and differential blood counts were carried out 2 to 4 times a month during the first 2 months, then, as a rule, once monthly. In view of the grave prognosis in granulocytopenia, patients treated with substances which can cause this complication should be given reasonable safety. In 3 cases of granulocytopenia, with 200 or fewer granulocytes per cubic millimeter, originated during treatment with Mesantoin or Dimedion, the granulocyte count had gradually diminished during the preceding weeks. Routine blood control at 4-week intervals is believed essentially to increase the chance of demonstrating a beginning granulocytopenia. In many cases an apparently harmless granulocytopenia will be found, with spontaneous remission, but such a finding should always occasion repeated blood cell counts at short intervals if administration of the preparation in question is continued. Clinical observation and instruction of patients as to the symptoms in severe granulocytopenia (fever, sore throat, tendency to abnormal bleeding) are necessary but not sufficient, since a severe granulocytopenia can appear without clinical symptoms. Treatment with Mesantoin and Dimedion should be introduced only when other antiepileptics have been tried.

Hydrosaline Disorders in Familial Periodic Paralysis. M. Espinar Lafuente, A. Sánchez Agesta, J. Díaz Nogales and E. de Landázuri. Rev. clín. españ. **71**:86-92 (Oct. 31) 1958 (In Spanish) [Madrid].

A man, 26 years old, was hospitalized at the medical clinic of the University of Granada, requesting treatment for recurrent crises of familial periodic paralysis from which he had been suffering for the past 6 years. The paralytic crises were more or less severe, involving mainly the legs and to a moderate extent the arms and being associated with nausea and vomiting. They subsided within 24 hours, leaving a sensation of great muscular weakness in the limbs. The clinical and biochemical examination of the patient in the periods when he was free from these attacks gave normal results.

In studying this patient, an artificial paralytic crisis was induced by the intramuscular injection of desoxycorticosterone acetate (DOCA) which was administered at 12-hour intervals in doses of 10 mg. per injection up to a total of 5 injections. The crisis appeared 9 hours after the 5th injection of DOCA. It lasted 30 hours, after which the sensation of muscular weakness was reported by the patient. The stage of induction of the crisis lasted 6 hours (2 before and 4 after paralysis was established). It was marked by hypopotassemia, hypernatremia, and abundant diuresis, the urine containing a large quantity of sodium. The sodium-potassium ratio was high and became still higher during the peak of paralysis which lasted 24 hours. This stage was marked by a progressive lowering of sodium and potassium blood levels, the sodium returning to a normal value and the potassium to a still lower figure. Recovery was marked by profuse diuresis, with a large quantity of sodium in the urine and a moderate amount of potassium. The sodium-potassium ratio was increased, with the potassium blood level returning to normal. This stage was prolonged for several hours after termination of the crisis. Normal elimination of potassium in the urine and normalization of the sodium-potassium ratio occurred on the second day after termination of the crisis. Calcium and creatinine in the blood were at normal levels.

The authors believe that their observations in this case, and those previously reported in the literature, confirm the fact that crises of familial periodic paralysis are due to disorders of the metabolism of electrolytes and water, with consequent

primary sequestration of potassium in the cells of the skeletal muscles and secondary sequestration of sodium.

Suicide and the Medical Community. J. A. Motto and C. Greene. A. M. A. Arch. Neurol. & Psychiat. 80:776-781 (Dec.) 1958 [Chicago].

The authors investigated the degree of contact that suicidal persons had with the medical community, before making a suicide attempt, in 175 consecutive suicides and in 197 unsuccessful suicide attempts in San Francisco between November, 1956, and September, 1957. At least 74 (42%) of the persons who committed suicide and 116 (60%) of those who attempted suicide were under medical care or had been so during the 6 months preceding the suicidal act. The physicians involved in the reports of the 372 persons represented all major medical specialties, except pediatrics; psychiatrists, general practitioners, and internists accounted for 47% of the 227 physicians known to have treated these patients. The patients complained most frequently of nervousness, depression, insomnia, abdominal distress, headache, apprehension, and seizures. Routine postoperative follow-up and antepartum and postpartum care also demanded attention as situations preceding a suicide attempt. Of the 372 persons, 84 (23%) had been in touch with a physician for at least a month before the suicidal act. Fifty-nine persons (16%) committed the act within a week of the last medical contact, and 14 (4%) had done so on the same day the physician was seen. Another 147 persons (40%) had seen a physician within 6 months of the suicidal act. Thus, the medical community is seen to be extensively involved in the suicide problem. The degree and kind of contact between members of the medical community and suicidal persons, and especially the physician's anxieties about suicide, are suggested as factors that should be studied further in assessing the physician's role in suicide prevention.

Psychic Symptoms in "Asia Disease." F. Askevold and A. Skulstad. Tidsskr. norske laegefor. 78:1066-1067 (Nov. 1) 1958 (In Norwegian) [Oslo].

Eight cases are described in which the psychiatric illness, for which the patient was admitted, seemed to develop after an acute febrile disorder in the fall of 1957, regarded as Asian influenza. In 4 patients episodes of mental symptoms had occurred previously, and hence the Asian influenza was considered as a precipitating factor. In 2 patients with protracted convalescence antibodies against the virus of Asian influenza could not be demonstrated. In 2 patients there was evidence of encephalitis, with marked schizophreniform symptoms.

GYNECOLOGY & OBSTETRICS

Chlorothiazide in Edema of Pregnancy. R. Landesman, R. N. Ollstein and K. J. Quinton. New York J. Med. 59:66-70 (Jan. 1) 1959 [New York].

Chlorothiazide (Diuril) was given to 100 pregnant women with edema in the toxemia clinic of the New York Lying-In Hospital. Of the 100 patients, 17 had preeclampsia, 27 had chronic hypertension without superimposition of acute toxemia, 16 had superimposition of acute toxemia, and 40 were normal. The drug was administered orally in doses ranging from 0.5 to 1.5 Gm. per day, the usual amount being 1 Gm. per day, given in divided doses of 0.5 Gm. The first tablet was given on arising and the second tablet in the afternoon so as to afford the patient an uninterrupted sleep, since the diuresis was then usually completed before retiring. The usual course of therapy was 7 days. However, some patients received chlorothiazide daily for several months. In rare cases administration of 1 Gm. of the drug per day produced nausea sufficient to require reduction in dosage to 0.5 Gm. per day with subsequent disappearance of symptoms. When diuresis did not follow the administration of 1 Gm. of chlorothiazide per day, the dose of the drug was increased to 1.5 Gm. per day. Seventeen patients received 1 mg. of reserpine daily, together with chlorothiazide. Four patients received 250 mg. of acetazolamide (Diamox) per day for one week.

All the patients responded to chlorothiazide with an initial weight loss, most marked during the first week of therapy. In the presence of clinically detectable edema, the agent was universally effective. The response was about proportional to the amount of edema initially present. Some patients showed an initial weight loss, but on prolonged therapy the diuretic response lessened, and a gain in weight occurred. In most patients diuresis diminished on sustained therapy when an apparent low-weight level was reached. Further increase in dosage had no effect in promoting diuresis. None of the patients accumulated massive edema fluid while receiving the drug. The patients with uncomplicated chronic hypertension showed a significant drop in blood pressure in response to chlorothiazide. The combination of chlorothiazide and reserpine appeared to enhance the hypotensive effect. With the onset of an acute process the antihypertensive effect of chlorothiazide was negligible when at all present. Chlorothiazide did not display apparent ability to reverse the toxemic process, since it did not reduce either fetal loss or the incidence of small babies. Chlorothiazide is a safe, potent, orally administered diuretic. The optimum daily dose is 0.5 Gm. given twice daily. On a balanced low-salt diet, chlorothiazide may be administered for periods up to 4 months without significant toxicity resulting to mother or fetus.

Problems in Diagnosis and Causes of Hirsutism. M. J. Fairweather and J. W. Goldzieher. J. Am. M. Women's A. **13**:501-509 (Dec.) 1958 [New York].

The classification of the causes of hirsutism in women presented by the authors lists 4 principal groups: (1) adrenal causes, which include hyperplasia and adenoma and carcinoma of the adrenals; (2) ovarian causes, which include (*a*) different masculinizing tumors, such as arrhenoblastoma, adrenal rest type (masculinovoblastoma), hilus-cell Leydig-cell tumor, and luteoma and (*b*) the Stein-Leventhal syndrome; (3) familial form of hirsutism, without recognizable endocrine disorder; and (4) iatrogenic form (induced by androgen therapy). To explain the endocrine basis of hirsutism in adrenal hyperplasia, the authors discuss the mechanism of the pituitary-adrenal axis. They also mention the newer techniques of urinary steroid studies and the range of 17-ketosteroids under normal conditions and in the various conditions that may lead to hirsutism.

To illustrate situations that may be observed in the differential diagnosis of hirsutism, the histories of 6 patients are presented. The first patient, a 33-year-old woman, had adrenal cortical hyperfunction (Cushing's syndrome) with marked hirsutism. Adrenalectomy was performed on the left gland, and a gray encapsulated tumor, measuring 10 cm. in diameter, was removed. Histologically, the tumor cells resembled those of the adrenal cortex. Five months after the operation the patient felt well, and since then has given birth to 4 living infants. In the second patient, in whom hirsutism resulted from an adrenal rest tumor of the ovary, a large (8 by 8 cm.), pedunculated, nodular tumor of the left ovary was removed. The third patient had the Stein-Leventhal syndrome, showing round face, beard, and extreme degree of frontoparietal baldness. At operation, the uterus was found to be 3 or 4 times the normal size, and the ovaries appeared large and cystic. The uterus, tubes, and ovaries were removed. Under ordinary circumstances, that is, in the absence of uterine carcinoma, wedge resection of the ovaries is usually sufficient in the large majority of women with the Stein-Leventhal syndrome.

In the fourth patient, a 60-year-old woman, exploration of the pelvis revealed a pedunculated fibroid on the uterine fundus and an intramural fibroid on the right side of the fundus. The ovaries were bound down, small, and atrophic. After myomectomy a bilateral salpingo-oophorectomy was done. The patient bled briskly, and the blood pressure fell but was restored with levarterenol bitartrate. As the bleeding could not be controlled, a hysterectomy was performed. The patient was discharged from the hospital on the 9th postoperative day. Microscopic sections revealed a small ovarian tumor nodule, composed of small lobules containing oval-to-round hyperchromic and vesicular nucleated cells with light gray to pink cytoplasm. These were diagnosed as Leydig-cell rests. The history of the fifth patient, a 25-year-old woman, illustrates the difficulties encountered in making the diagnosis of familial hirsutism. This patient had a family history of excess hair growth and, although showing some menstrual disturbance, gave evidence of ovulation. On the basis of urinary steroid studies, the authors conclude that a mild degree of adrenal hyperplasia was present, superimposed on a strong family history of hirsutism. The sixth patient had adrenal hyperplasia that responded to cortisone therapy.

Primary Cancer of the Vulva. Ann. chir. et gynaec. Fenniae (supp. 5) **47**:17-29, 1958 (In English) [Helsinki].

A series of 182 patients with primary carcinoma of the vulva were treated at the Institute of Radiotherapy, University of Helsinki. The patients were classified into 2 groups: one consisted of 153 patients who had not received treatment prior to their admission to the institute, and the other consisted of 29 patients who had had treatment at another hospital. The patients of the first group presented different stages of the disease; in one-fourth of the patients it was too widespread to attempt any therapeutic measure. Several patients of the second group had cancer, grade 1. Relapses and metastases occurred in more than one-half of the patients. Of the 153 patients belonging to the first group, 116 were amenable to treatment, and 98 of these were subjected to local electrocoagulation. The inguinal lymph nodes were treated by means of teleradium therapy or roentgenotherapy in two-thirds of the patients, but no such treatment was applied to this region in the remaining one-third. The 5-year survival rate was 36.1% among the 98 patients who were subjected to electrocoagulation, 27.5% among the 153 patients who had had no treatment before admission, 42.1% among the 145 treated patients, and 60.5 to 65.5% among the patients with cancer, grade 1. In addition to electrocoagulation, other local treatments, such as surgical extirpation of the tumor, treatment by means of a radium plate or by intubating radium needles, teleradium therapy, or roentgenotherapy, have also been used. This study illustrates the importance of early treatment of patients with carcinoma of the vulva, which constitutes no exception from other types of carcinoma.

Formal Carcinogenesis in the Uterine Cervix. H. G. Hillemanns. Arch. Gynäk. **191**:235-270 (No. 3) 1958 (In German) [Munich, Germany].

The formal genesis of beginning tumor growth is just as problematical as is its causation. The question whether certain tissue changes are neoplastic

or preneoplastic is of fundamental importance for the evaluation of the surface carcinoma of the uterine cervix. It is closely allied to two other questions, namely, whether this cancer must be traced to unicentric germination of the tumor anlage or to multicentric foci, and whether one is to expect a monophasic or a polyphasic growth. The author traces the various steps in the formal carcinogenesis in the uterine cervix. He himself performed all histological studies on material obtained from the clinic and from a cancer detection center in connection with colposcopic and cytological studies at the women's clinic of the University of Freiburg. In the course of the 5 years from 1953 to 1957, studies were made on 84 surface carcinomas, 24 microcarcinomas, and 638 cervical carcinomas in stages 1 to 4 (including microcarcinomas); also in 30 cases with unstable epithelium and in 26 with atypical epithelium, cases which are being watched and are still inconclusive.

The simultaneous appearance of surface carcinomas with erythroplasia, as well as similar local conditions on the external female genitalia, justifies the classification of surface carcinoma as a precancerosis. With exact observation, multicentric development can be demonstrated in 25% of the cases. In the majority of cases carcinogenesis is a unilocular process at the epithelial border of the cervix. Multiple genesis corresponds to the results of experimental cancer production and coincides with the field theory described by Willis in 1944-1945 and in 1953. The author mentions the possibility of the appearance of multicentric foci, as well as the misinterpretation of recurrences and metastases.

The tumor anlage is of multicellular origin; this is proved by multicentric foci and varying types of carcinoma on adjoining matrixes. Whether further dissemination takes place only by proliferation or also by inductive modification is still being discussed. As is proved by the study of microcarcinomas, the growth of true cancer originates from several sites of the preneoblastic surface epithelium, that is, it is pluricentric. Experimental tumor formation takes place in several phases and resembles a gradual dedifferentiation. Biphasic growth can be proved in cervical cancer as it has been in the dermatological precanceroses.

Biological studies demonstrated that the transition from the normal-appearing to the cancerously degenerated cell takes place gradually over a period of time, not in sudden leaps; the process can be followed morphologically. Cancer formation in the cervix is likewise a chronic process with prolonged latency. However, after a certain threshold value has been reached, infiltration occurs in a short time. On the basis of his own experiences and of the critical evaluation of previous reports, the author believes that, as regards the cervix, the morphologically monophasic carcinoma, developing directly and without latency, is without significance. Spontaneous regressibility of a surface carcinoma (established on the basis of strict criteria) does not seem to have been proved, and can be expected only after a change in the milieu.

The author emphasizes the decisive importance of the method of securing and processing tissues for the evalution of the growth of cervical carcinoma. After commenting on pathological and gynecologic viewpoints, he assumes a gradual increase in the malignancy in cervical carcinoma, in accordance with the biphasic mechanism in experimental carcinogenesis and with the demand for multiple cancer cells for tumor formation. In Druckrey's scheme of precancerosis, surface carcinoma is defined as the early stage of a malignant process which is still of purely cellular character.

Detergents in the Treatment of Leukorrhea. P. Godts. Belg. tijdschr. geneesk. 14:1085-1092 (Nov. 15) 1958 (In Flemish) [Leuven, Belgium].

According to Godts, detergents are widely used in the treatment of leukorrhea resulting from vaginal infections. He defines detergents as substances capable of reducing the surface tension of water, and discusses their characteristics. After describing the isolation of Candida albicans from the vaginal smears of patients with leukorrhea, he reports studies on the effects of various solutions of the detergents, Sabenyl and Neo-Sabenyl, on cultures of C. albicans isolated from such smears. The therapeutic use of detergents consists in, first, cleansing the vagina with a tampon containing a detergent solution; then a tampon that has been saturated with 5% solution of detergent is inserted into the vagina and is left in place for from 12 to 24 hours; this is followed by daily vaginal irrigations with a detergent solution for one week.

The 90 patients with leukorrheal vaginitis, treated with detergents and reviewed in this paper, included 30 with infections due to C. albicans (which are especially frequent in pregnant women), 30 with trichomoniasis, and 30 with mixed infections. Although the importance of Trichomonas vaginalis as a cause of infection has not been definitely established, when these parasites disappear from the vagina secretions after treatment, the clinical symptoms subside. The term "mixed infection vaginitis" was applied when either, both, or neither of C. albicans and T. vaginalis are found together with bacterial organisms. Treatment with detergents produced excellent results in 71 of the 90 patients—in 26 of those with moniliasis (C. albicans), in 24 of those with trichomoniasis, and in 21 of those with mixed infections. Good results were obtained in 9 additional patients (including 5 with

mixed infections), whereas in the other 10 patients the effects of treatment with detergents were poor. On the basis of these results, the author recommends the use of detergents in the aforementioned forms of leukorrheal vaginitis.

Clinical Significance of the Enzymatic Study of the Ascitic Fluid in Maligant Tumors of the Ovary. G. Santoni. Minerva ginec. **10**:677-681 (Sept. 15) 1958 (In Italian) [Turin, Italy].

The author studied the lactic dehydrogenase activity in the ascitic fluid of 15 women with malignant tumor of the ovary, in 10 women with no tumor, and in some normal women. The values of this activity in the ascitic fluid of the 15 women with ovarian tumor were much higher than the values obtained in patients without tumor and in the normal women. The author believes that the lactic dehydrogenase activity is the result of the enzyme present in the necrotic parts of neoplastic tissue. The high lactic dehydrogenase activity, in fact, was present in patients with malignant tumor of the ovary already in an advanced stage. The values of the lactic dehydrogenase activity in the blood serum of women with malignant tumor of the ovary were found to be lower than the values of this activity in the ascitic fluid; therefore, the author believes that the enzyme present in the ascitic fluid does not derive from the blood.

The Conservative Operation for Endometriosis: A Report of Its Use in 200 Cases. L. A. Gray. J. Kentucky M. A. **56**:1219-1225 (Dec.) 1958 [Louisville].

The author reports on 200 women, between the ages of 18 and 40 years, who underwent the conservative operation for endometriosis. One hundred fifty-three patients (76.5%) were less than 30 years of age. Forty-seven patients were unmarried, 153 were married, and 28 (18.3%) of the latter had had children previously. The chief complaints of the patients were dysmenorrhea in 86.5%, sterility in 50.5%, intermenstrual pelvic pain in 33%, menometrorrhagia in 32.5%, and dyspareunia in 25.5%. One hundred twenty-nine patients (64.5%) had retroversion of the uterus. The conservative operation for endometriosis is a distinct one in gynecology, including dilatation of the cervix and curettage, excision of endometrial implants, resection of endometrial cysts, and suspension of the uterus. The approach was through a midline incision. Presacral neurectomy was performed in 44 patients (22%) who had the more severe dysmenorrhea. Myomas were excised in 31 patients. Modified Gilliam suspension of the uterus was performed on 178 patients.

There were no deaths and no obstructions. Subsequently 57 of the 200 patients became pregnant. Of 49 patients specifically complaining of sterility, treated in the past 10 years, 25 (51%) became pregnant. The relief of dysmenorrhea, pelvic pain, dyspareunia, and menometrorrhagia was gratifying. Six of the 200 patients have had secondary radical operations. The conservative operation for endometriosis requires care, tedious dissection, and often more time than hysterectomy. The results obtained confirm the impression that this operation is a satisfactory and proper method of treatment when it is strictly indicated because of disabling symptoms or because of sterility which does not respond to usual conservative procedures. It should not be performed though, until the patient has been observed and surgical intervention seems clearly necessary. In case of realization and necessity of a second laparotomy later, the conservative operation for endometriosis should not be considered a failure if normal health has intervened for a number of years or if pregnancy has occurred.

Delay by Physician and Patient in the Diagnosis and Treatment of Pelvic Cancer. C. E. Flowers Jr., R. A. Ross and N. L. Pritchett. South. M. J. **51**: 1497-1504 (Dec.) 1958 [Birmingham, Ala.].

According to the American Cancer Society, 50% of those who die of cancer could be saved if patients and physicians would familiarize themselves with and use all available knowledge of the disease. During a 4-month period 191 patients with pelvic cancer were studied at the North Carolina Memorial Hospital in Chapel Hill to determine the preventable factors in their disease. The charts of 70 of these patients who died of pelvic cancer were also reviewed. The incidence of delay on the part of the physician to give a proper diagnosis, and of delay on the part of the patient to consult a physician after the occurrence of the first symptoms of pelvic cancer, was established according to the Philadelphia Plan for Pelvic Cancer Control. It was evident that almost none of the patients had been advised by their physicians to have annual physical examinations. There were many patients who failed to report symptoms of pelvic cancer to their physicians, as well as an unfortunately large number of physicians who neglected to establish the diagnosis of pelvic cancer and to institute treatment. Delay in consulting a physician was found among 42% of the patients with carcinoma of the cervix, with an average delay period of 18 months. Delay in establishing a proper diagnosis was found among 19% of the physicians, and the average time elapsed between the patient's first visit to the physician and the establishment of the correct diagnosis was 9 months. Delay on the part of both patient and physician was found to be 14%, with an average delay period in consulting a physician and/or establishing a correct diagnosis of 14 months. Fifty-four per cent of the patients with invasive carcinoma of the cervic had no symptoms 6 to 12 months prior

to consulting their physicians. Of the 46% who could have had their disease diagnosed before it became advanced, 16% delayed their visits to the physicians, and in 30% the physicians failed to make a proper diagnosis. Sixteen per cent of the patients with carcinoma of the endometrium delayed their visits to the physicians, and in 20% of these the physicians failed to make a correct diagnosis.

One cannot expect much improvement regarding delay in diagnosis and treatment until one impresses upon the public and the profession that in the majority of patients curable cancer is asymptomatic. The incidence of pelvic cancer can be materially reduced by physicians' stressing the importance of annual physical examinations and by the establishment of state and county committees for the study of pelvic cancer.

Cancer of the Cervix: Prevalence, Special Surgical Technique, and Evaluation of Results. S. Mitra. Cancer **11:**1190-1194 (Nov.-Dec.) 1958 [Philadelphia].

The anatomic distribution of cancer is not the same in different parts of the world. In a diagram the author shows the comparative incidence of cancer of different sites among patients in 2 institutions, the Cancer Hospital of Calcutta and the Royal Cancer Hospital of London. The preponderance of oral, laryngeal, and cervical cancer is marked in India. Cancer of the cervix constitutes 23.3% of all cancers in Indian women. This form of cancer was believed to be rare among Mohammedan women, but, in comparing the incidence of cervical cancer among Hindus and Mohammedans, the author found it to be practically the same. He believes that it is not the ethnological difference but the habits and the environment, the social status, and the assaults on the cervix from repeated childbirths that are responsible for the frequency of cancer of the cervix. There is no racial susceptibility to this type of cancer.

The author has been concerned with cancer of the cervix since 1924. During the early years of this period he treated all cervical cancers with irradiation therapy, as was then customary, but the first 5-year end-results were not encouraging, the cure rate being only 16.6%. Since then he has combined surgical with irradiation therapy. He resorted to Schauta's radical vaginal hysterectomy in preference to Wertheim's operation, because in India the primary mortality rate was much higher in Wertheim's than in Schauta's operation. There was only one ureteral fistula in a series of 391 patients operated on. Comparative 5-year end-results for patients with cervical cancer of stages 1 and 2 indicated better salvage with radical surgery (65.6%) than with irradiation therapy (43.5%). Postoperative complications were minimal with the author's technique of extraperitoneal lymphadenectomy and radical vaginal hysterectomy. Pelvic node metastases were found in 23.2% of the patients with cervical cancers in stages 1, 2, and 3 (38 of 164 in the newest series). The parametrium was rarely infiltrated; there was parametrial involvement in only 1 of 38 patients with metastases in the pelvic nodes.

The author concludes that the surgical method he employs in cervical cancer has definite advantages. This is substantiated by a 5-year salvage rate of 70% in patients with cervical cancers in stages 1, 2, and 3. Five-year survival has reached 84.6% for women in whom the pelvic nodes are not involved, compared with 43% for the group with metastatic cancer in the pelvic nodes.

Twin Pregnancy in a Uterus Didelphys: A Case Report. W. M. Dawson and W. H. Ainslie. J. M. Soc. New Jersey **55:**649 (Dec.) 1958 [Trenton].

The authors present the history of a 22-year-old primigravida who was first seen on March 1, 1957. Her last menstrual period had been on Jan. 9, and her expected date of confinement was Oct. 16. Her antenatal course was uneventful until July 3, when palpation revealed the probable presence of a twin gestation and "double" uterus. There was a vertical midline groove on the uterus, giving an irregular "U" effect, with a distinct fetal heart in each limb of the "U." The patient went into labor spontaneously at 32 weeks of gestation. The first twin, a living male infant weighing 1417.5 Gm. (50 oz.), was delivered from the right uterus. The intact placenta was expressed spontaneously 5 minutes later.

At this time, the cervix of the left uterus was fully effaced and dilated to 4 cm., with bulging membranes which were ruptured artificially. Contractions continued irregularly and weakly in the left uterus. An infusion of oxytocin was begun with good results, and the second twin, a living male infant weighing 1615.9 Gm. (57 oz.), was delivered from the left uterus. The intact placenta was expressed 5 minutes later. Subsequent bleeding was minimal, and the patient's postpartum and puerperal course was uneventful. Both infants survived. The authors say that premature termination of pregnancy is usual in cases of double ovum twins, each twin residing in a separate half of a uterus didelphys, but the survival of such twins is extraordinary.

PEDIATRICS

Physiologic Abnormalities of Salicylate Intoxication. W. E. Segar and M. A. Holliday. New England J. Med. **259:**1191-1198 (Dec. 18) 1958 [Boston].

Forty-nine children were seen and treated for salicylate intoxication at the James Whitcomb Riley Hospital, Indianapolis, between 1952 and 1957. All

were less than 6 years of age. Two were being treated for rheumatic fever. Of 43 with a history of salicylate ingestion, 11 children obtained the drug themselves or were fed it by an older sibling. The remaining 32 poisonings, primarily involving children under 2 years, were due to misguided therapeutic efforts of the parents, often upon the advice of a physician. There were 5 deaths, all in children less than 2 years of age; all 5 had severe hyperpyrexia. Eight children, of whom 6 were less than 2 years of age, had convulsions. The authors give particular attention to the metabolic alterations produced by salicylates. Hyperthermia, which is a prominent and occasionally a lethal result of salicylate intoxication, cannot develop unless the normal heat-regulating mechanisms are impaired. Since these mechanisms depend, in part, upon the evaporation of water from the skin and lungs, they are compromised by dehydration, which is observed in all children with serious salicylate intoxication. Both hyperventilation and sweating result in increased water and electrolyte expenditure. Vomiting and diarrhea occur frequently and contribute to the dehydration. Once the body water stores are depleted, salicylate can no longer induce effective sweating, and its hyperpyretic action is no longer balanced by effective defenses. Thus, hyperpyrexia accelerates dehydration, and dehydration potentiates hyperpyrexia. The greater loss of water than of electrolytes will result in hypernatremia.

Hyperglycemia occurred in 4 of the 14 children on whom appropriate studies were made. Salicylates have several separate pharmacological actions that alter carbohydrate metabolism. They increase "glucose demand," as well as the rate at which glucose is absorbed from the gastrointestinal tract; they probably increase the rate of production or of release of adrenal corticoids; and they interfere with the processes by which glucose is metabolized. Only the increase in glucose demand tends to lower blood sugar; the remaining 3 actions tend to produce hyperglycemia and glycosuria. The alterations in the carbohydrate metabolism also contribute to the production of ketosis. The urine of 30 children was examined for ketone bodies, and 27 of these tests were positive. Attention is called to the severe disturbances in the pH of the body fluids, including the early occurrence of a respiratory alkalosis, which is followed by a metabolic acidosis. The respiratory alkalosis is rarely of clinical importance except that it depletes the patient's buffering capacity and cation reserves for the acidosis that will follow. The various factors contributing to the metabolic acidosis, including abnormalities in carbohydrate metabolism and the production of ketosis, are reviewed.

Hyperthermia and dehydration are the immediate threats to life, and the initial therapy must be directed at their correction. External cooling with water or alcohol should be provided quickly to any child who has a rectal temperature over 104 F (40 C). Intravenous infusions of fluids must be prompt, because the patient's defense against hyperpyrexia can function only after the dehydration has been corrected. Electrolyte therapy, but not water, may be withheld until the presence of a metabolic acidosis can be confirmed and until the presence or absence of hypernatremia can be ascertained. Intravenous infusions of fluids similar to those that would be prescribed for a diabetic patient in acidosis should be planned for the succeeding 24-hour period. If the child is in shock or in impending shock, 20 to 30 ml. of Ringer's lactate solution per kilogram of body weight should be given rapidly before the 24-hour therapy is started. The initial fluids should contain no potassium. Other supportive measures may include the liberal parenteral administration of vitamin C and vitamin K.

A Controlled Study of Beta Hemolytic Streptococcal Infection in Rheumatic Families: I. Streptococcal Disease Among Healthy Siblings. J. M. Miller, S. L. Stancer and B. F. Massell. Am. J. Med. **25**:825-844 (Dec.) 1958 [New York].

Data on the incidence of hemolytic streptococcic infections in 235 healthy children, between the ages of 5 and 16 years, who belonged to families that included at least one sibling with a definite history of rheumatic fever were collected from September, 1953, to June, 1956, at the House of the Good Samaritan, Children's Medical Center, Boston. Throat cultures and antistreptolysin O antibody levels served as the laboratory means of documenting all symptomatic streptococcic illnesses as well as asymptomatic streptococcic carrier states. Of 603 symptomatic respiratory illnesses occurring among the 235 children, 14% were associated with beta-hemolytic streptococci, and 90% of these organisms were of the group A variety. The most frequent clinical category of respiratory disease encountered was coryza which was rarely accompanied by laboratory evidence of streptococcic infection, whereas tonsillopharyngitis was the second most frequent clinical entity and showed a correlation with group A streptococci of 30%. Isolated fever was particularly associated with streptococci, and fever generally seemed to be the most important correlative finding of symptomatic streptococcic infection. Fully 55% of all group A hemolytic streptococcic infections observed were asymptomatic carrier states detected in children who were presumably well. Of the 603 symptomatic respiratory illnesses, 169 were group A hemolytic streptococcic infections. The diagnosis of group A hemolytic disease was made by positive culture in 157 (93%) of the 169, whereas immunological response alone was the basis for diagnosis in 12 (7%). Many different

serologic types of group A organisms were detected among 151 isolations which were typed. Type 6 was most frequently encountered among the strains which could be typed. Of the 151 organisms studied, 53 (35%) could not be typed with the antiserums available. Suitable data on antistreptolysin O were available from 129 (76%) of the 169 group A hemolytic streptococcic infections observed, and a significant antibody rise was detected in 51 (40%) of the 129, of both symptomatic and asymptomatic groups of illnesses. The frequency of antibody response in the various categories of symptomatic streptococcic infection was about the same. Although the frequency of a significant antibody response seemed related to the numbers of streptococci in the throat, antibody rises occurred in the absence of positive throat culture in some cases. The 40% incidence of antibody response occurred in spite of early diagnosis and fairly prompt penicillin treatment of most such bacteriologically documented infections.

Three regimens of penicillin treatment were studied. An oral 10-day regimen of buffered penicillin G in a daily dose of 400,000 units was found to be suppressive for beta-hemolytic streptococci while the drug was administered, but bacteriological relapse occurred in 6 (30%) of 20 patients who received this treatment. A 10-day course of orally administered buffered penicillin G totalling 1.2 million units daily was highly effective in treating patients with symptomatic infections, was somewhat less effective in eradicating the carrier state, and was a failure in 9 (13.8%) of 65 patients so treated. A single intramuscular injection of 600,000 units of benzathine penicillin G failed in 4 (9.1%) of 44 patients. The oral program of treatment was well tolerated, with complete absence of side-effects of allergic reactions. The intramuscular preparation was tolerated with freedom from allergic reactions, but patients did complain of transient pain at the site of injection. Although no overt indication of typical rheumatic fever was seen after these 169 streptococcic infections, 2 instances of rheumatic heart disease appeared insidiously, and 1 instance of erythema marginatum was detected. The general occurrence rate of hemolytic streptococcic disease was greater among children of this study who still had their tonsils than among those whose tonsils had already been removed.

A Controlled Study of Beta Hemolytic Streptococcal Infection in Rheumatic Families: II. Penicillin Prophylaxis among Rheumatic Fever Subjects, Comparing Different Regimens. J. M. Miller, S. L. Stancer and B. F. Massell. Am. J. Med. 25:845-856 (Dec.) 1958 [New York].

The authors report on observations made during the period from 1953 to 1956 at the House of the Good Samaritan, Children's Medical Center, Boston, concerning the effectiveness of penicillin in the prevention of group A hemolytic streptococcic infections among children who were convalescing or who had completely recovered from acute rheumatic fever. A group of 452 hospitalized patients with acute rheumatic fever or a definite history of rheumatic fever received 200,000 units of buffered penicillin G given orally twice daily over the 3-year period. Another group of 114 rheumatic outpatients received 200,000 units of buffered penicillin G given orally twice daily, and 47 rheumatic outpatients received 1.2 million units of benzathine penicillin G intramuscularly at 4-week intervals. Healthy siblings of both outpatient groups of rheumatic children did not receive prophylactic penicillin and served as controls for measuring the incidence of streptococcic disease in these particular family environments.

No instances of recurrence of rheumatic fever developed among the entire group of 452 hospitalized patients, and in only 2 of these children did asymptomatic carrier states with group A streptococci develop. There was no case of elevation of antistreptolysin O among the entire group. There were 2 definite recurrences of rheumatic fever among the 114 rheumatic outpatients who received orally 200,000 units of buffered penicillin G twice daily, and there were no recurrences among the 47 rheumatic outpatients who were given 1.2 million units of benzathine penicillin G intramuscularly every 4 weeks. The oral regimen of prophylaxis achieved a striking reduction in streptococcic infections among the ambulatory outpatients receiving penicillin, as compared with their healthy siblings who were not so protected, and the intramuscular administration of long-acting penicillin showed even greater efficacy as a prophylactic agent. Among the 452 hospitalized rheumatic patients who received the continuous prophylactic amount of 200,000 units twice daily, there were only 3 with an untoward reaction of pruritic rash which required discontinuation of the penicillin preparation. None of the 114 outpatients showed adverse effects attributed to penicillin given orally. Subjective reactions among the patients who received penicillin intramuscularly were frequent. The reactions necessitated termination of this form of prophylaxis in 4 of these patients.

The results of this study have demonstrated the superior prophylactic benefit of repository injectable penicillin, but the risk of reactions has been greater than that associated with penicillin given orally. Oral therapy with penicillin is an effective agent in the prophylaxis of streptococcic disease, but continued cooperation by the patient is required in taking the drug by mouth. Both regimens have appropriate usefulness in the prevention of recurrences of rheumatic fever.

A Case of Cushing's Syndrome in an Infant. E. Goldblatt and A. H. Snaith. Arch. Dis. Childhood **33**:540-542 (Dec.) 1958 [London].

The child presented was a girl, born after a normal pregnancy, who appeared normal when she was one year old. Two months later she was brought to hospital because of rapid gain in weight and increasing irritability. She was obese, with a buffalo hump, her face was plethoric, and she had an acneiform rash. There was slight hirsuties of the face and back. No striae were present. An intravenous pyelogram suggested enlargement of the right adrenal, and studies on the excretion of steroids revealed greatly increased values. In the expectation that an adrenal tumor would be found, an exploratory laparotomy was undertaken. Cortisone was given orally for 2 days prior to the operation. Both adrenals were found to be slightly enlarged and nodular. The left adrenal was removed, and after further investigation it was decided to remove the right adrenal. In preparation for the second adrenalectomy, cortisone was given orally and intramuscularly. The postoperative course was uneventful, the cortisone dosage was gradually reduced, and the patient was discharged 2 months later, by which time her appearance had become much more normal. At present she is on maintenance therapy with 20 mg. of cortisone acetate and 1 Gm. of salt a day. Three months after discharge the patient was again admitted to hospital, suffering from avulsion of 2 finger tips which had been caught in a train door. She withstood this trauma without any evidence of metabolic upset. The authors believe that this is the first time that adrenalectomy has been performed on an infant with adrenal cortical hyperfunction (Cushing's syndrome). The long-term prognosis remains to be seen.

Fourteen Personal Cases of Pneumocystis Carinii Pneumonia. G. Berdnikoff. Canad. M. A. J. **80**:1-5 (Jan. 1) 1959 [Toronto].

The author reports on 7 male and 7 female infants with pneumonia due to Pneumocystis carinii, who were treated and who died at 4 hospitals in Canada between 1930 and 1958; the ages of the patients ranged from 2 to 4 months at the time of death. The clinical histories of the 3 most recent cases are summarized; these reflected rather faithfully the clinical aspect in all 14 patients whose lungs microscopically presented a typical picture of Pneumocystis pneumonia. Both sexes were equally affected. Four of the 14 infants were premature. Debility, whether due to prematurity or to other causes, seemed to be of major importance. The illness started with a sudden onset of periods of dry, unproductive cough accompanied by signs of suffocation. Cyanosis and polypnea were rather pronounced, and there was marked sternal retraction. Administration of oxygen usually brought relief, but symptoms recurred as soon as it was discontinued. There was no rise of temperature, except when the disease was complicated by another infection.

A symptom-free period of a few days' duration after the initial onset of the disease was definitely present in 7 of the 14 infants; it deserves special consideration, since it might become a valuable tool for the clinical diagnosis of the disease. The initial period of suffocation might be caused by edema and formation of hyaline pseudomembranes, which were well represented in certain regions of the lung of one of the patients, perhaps due to some hyperergic reaction. The disappearance of the exudate associated with pseudomembranes might then explain the remission of symptoms for a few days. This would be followed by new periods of suffocation, which now, however, were due to the direct obstruction of alveoli and bronchi by masses of the pullulating Pneumocystis organisms. Further observations are necessary in order to evaluate the exact incidence of the "symptom-free period."

Spontaneous pneumothorax was not rare among these patients. White blood cell counts varied between quite high values, up to 28,000 per cubic millimeter, and surprisingly low values, such as 8,900 per cubic millimeter, and for this reason cannot be depended on. The x-ray picture of the lung did not permit differentiation from other conditions, such as milk-aspiration pneumonia. There was absence of air usually in the perimediastinal regions of the lung parenchyma, accompanied by emphysema usually in the peripheral regions. The question of epidemiology still remains unanswered. Needle biopsy of the lung appears at present to be the only possible way of establishing a positive diagnosis during life. Nonfatal cases certainly exist, and it is left to the ability of clinicians to find a specific treatment.

Some Psychological Contributions to the Clinical Treatment of the Asthmatic Child. A. Macedo De Queiroz and A. Strauss. Acta allergol. **12**:396-406 (no. 6) 1958 (In English) [Copenhagen].

The authors report on 40 children, between the ages of 2 and 11 years, with asthma who were admitted to the Hospital das Clínicas of the Medical School of the University of São Paulo, Brazil, and who were subjected to a specialized psychological study because of the close relationship between asthma and the personality of children. A clinical diagnosis of allergic asthma was the only factor in common of all the children in this group. They received medical treatment consisting of removal of specific allergenic factors and, when indicated, hyposensitization with allergenic extracts and autovaccines. Interviews were held with

the patient and his relatives, and the patients were observed in free activities and were given psychological tests. The results of the psychological investigation revealed the existence of psychological factors directly related to asthma as causative agents, psychological factors indirectly related to asthma, and behavior problems frequently observed in children with asthma.

Direct influences included emotional tensions, resulting from conflicts at home, punishments, school examinations, parties, new situations such as entering school or playgrounds for the first time, and the feeling of being unwanted or having lost affection. The "use" of the asthmatic attack as a means to obtain specific ends, such as a mother's special care and attention, should also be considered as a factor directly influencing the disease. As indirect influences, there should be considered factors related to the emotional environment of the home, such as overanxious and depressive parents, marital conflicts, or unstable financial situations, and factors due to wrong educational attitudes, such as overprotection and constant vigilance over the asthmatic patient. Behavior problems accompanying the asthmatic symptoms included aggressiveness in 39 patients, anxiety in 32, overdependence on the mother or other family members in 28, anorexia in 23, fears in 23, negativism and stubbornness in 18, jealously, withdrawal tendencies, temper tantrums, and sleep disturbances in 13. These problems reflected clearly emotional and educational situations, as 34 of the 40 children had normal intelligence levels.

Combined psychological and medical-allergic treatment not only brought real benefit to the child's personality but also caused a more rapid improvement of asthma in all the children. Consequently psychological investigation seems absolutely justified. Psychopedagogic orientation to be given to the family is outlined. Psychological treatment, referring to the child's necessities and his psychological problems, was focused on enrichment of his experiences, canalization of aggressivity or elimination of its causes, elimination of causes of fear, support of achievements, and small tasks of responsibility at home. A specialized psychological examination would seem perfectly justifiable in patients with large psychological interference and when the family environment permits it.

Staphylococcic Pneumonia in Infants: Six Cases. E. Jaso and L. Abarca. Rev. espan. pediat. **14**:663-676 (Sept.-Oct.) 1958 (In Spanish) [Saragossa, Spain].

Staphylococcic pneumonia is a severe and often fatal form of suppurative pneumonia which complicates some epidemics of influenza in infants. It is caused by Staphylococcus pyogenes var. aureus, which does not respond to treatment with sulfonamides, although it responds to chloramphenicol and to streptomycin. It may be complicated by (1) influenzal bronchitis, (2) a staphylococcic infection located at any distance from the respiratory tract, and (3) fibrosing pancreatitis. The early symptoms are those of pneumonia, with acute respiratory disorders: cough, dyspnea, fever, vomiting of hemorrhagic or purulent phlegm, and vascular shock. The roentgenograms of the chest are typical, showing innumerable pulmonary abscesses, both miliary and larger, up to 5 mm. in diameter. Most frequently the abscesses open into the pleura, causing empyema, pneumothorax, pyopneumothorax, or pneumatocele. Often there is a recurrence, with aggravation of the pneumonia.

Six cases of staphylococcic pneumonia in infants, between the ages of 1 month and 1 year, are reported. The predominant symptoms were typical of pneumonia in 4 cases and were similar to those of ileus in 1 and to those of pulmonary tuberculosis in 1. A diagnosis was made with certainty by the typical aspects of the lungs in roentgenograms of the chest, which showed unilateral pulmonary abscesses with pneumothorax or pneumatocele in 5 patients and bilateral pulmonary abscesses in 1. In all the patients there was polynuclear leukocytosis with intense nuclear deviation ("shift to the left"). Recovery was obtained through administration of erythromycin to 2 patients, of chloramphenicol to 2, and of streptomycin to 1. The patients with fibrosing pancreatitis and a pneumatocele died of recurrence of the pneumonia 4 months after the first attack.

Aminophylline Poisoning in Children. H. L. Bacal, K. Linegar, R. L. Denton and R. Gourdeau. Canad. M. A. J. **80**:6-9 (Jan. 1) 1959 [Toronto].

The authors report on 10 children, between the ages of 8 months and 10 years, with aminophylline (theophylline ethylenediamine) poisoning arising from the therapeutic use of the drug in the management of bronchial asthma and upper respiratory infection. The drug was administered by the rectal route to 8 patients and intravenously to 1; in 1 patient the route of administration was not ascertained. The total known dosage ranged from 3¾ grains (225 mg.) for a 4½-year-old child to 22½ grains (1,350 mg.) in 36 hours for a 3½-year-old asthmatic child. Irritability, vomiting, hematemesis, and dehydration were nearly always present and complicated the preexisting disease for which the drug was administered. Albuminuria, drowsiness, convulsions, and cardiovascular syncope also were observed in some of the patients. Treatment of the intoxication was purely symptomatic, aimed at sedation, support of respiration and circulation, and prompt correction of dehydration. All the patients recovered and were discharged from the hospital within 24 hours to 14 days.

Theophylline is the most active of the xanthine agents, and the combination with ethylenediamine makes it more soluble and more completely absorbed. The xanthines stimulate the central nervous system, augment gastric secretions, cause diuresis, and exert central and peripheral actions on the cardiovascular system. The clinical manifestation of overdosage of aminophylline may be central nervous system stimulation with unusual restlessness and irritability; this is an early sign and may progress to tremors, epileptiform convulsions, drowsiness, and coma. Prolonged increase in gastric secretion may be manifested by nausea, persistent vomiting, or even hematemesis. Increased urine output may be associated with reversible albuminuria and dehydration. Cardiovascular collapse or even death may result. To eliminate preventable iatrogenic intoxication, the authors recommend the following dosages in the oral and rectal administration of aminophylline for the treatment of bronchial asthma in children: (1) suspension tablets given orally: 1½ grain (5 mg.) per kilogram of body weight; the dose may be repeated every 8 hours, but not oftener than every 6 hours; (2) rectal suppository or retention enema: ⅛ grain (7 mg.) per kilogram of body weight; the dose may be repeated every 8 hours, but not oftener than every 6 hours, and is to be restricted to patients in whom oral administration is not practicable. No undesirable side-effects were observed at the Montreal Children's Hospital with this regimen, which has been found adequate for treatment of children with asthma exclusive of those in status asthmaticus.

UROLOGY

Unilateral Multicystic Kidney: Report on One Case. G. Conca and E. De Nicolai. Minerva pediat. **10:** 1097-1104 (Oct. 13) 1958 (In Italian) [Turin, Italy].

The authors report on a female infant with a unilateral multicystic kidney. At birth the child presented a mass which occupied the whole left flank; on the 5th day roentgenologic examination showed that the mass occupied the entire left side of the middle part of the abdomen and the uppermost part of the pelvis. The mass increased in size, and at the 8th month the child, who was otherwise in good condition, was operated on. A polycystic mass of the dimension of a small fetal head, occupying the whole left flank and part of the hypochondrium on the left, was isolated and enucleated. The mass substituted for the left kidney and showed some residue of parenchyma at the level of the hilus; the right kidney, the liver, and the pancreas showed no alteration. The mass was of a milk-white color and weighed 245 Gm. (9 oz.); its circumference was 21 cm. transversally and 26 cm. longitudinally. Structures identifiable as the vein and the artery of the kidney and a filamentous structure, a few centimeters long, without a lumen (probably an atresic ureter) were recognized. On section, the mass appeared to be composed of about 10 cystic formations of various dimensions and diameters. The cysts had a smooth surface and contained some clear watery liquid. The cystic cavities did not intercommunicate, and no excretory ducts were noticed macroscopically. Histological examination showed that the walls of the cysts were made up of connective tissue lined with cuboid epithelial cells. The tissue among the cystic cavities was made up of dense connective collagen. The child had a normal recovery, during which azotemia and urine tests gave normal values. Five months after the operation she was in good condition.

Evaluation of a Method for Detecting and Following Urinary Tract Infection in Females Without Catheterization. H. D. Riley Jr. J. Lab. & Clin. Med. **52:**840-848 (Dec.) 1958 [St. Louis].

It is generally accepted that urine specimens for evaluation of urinary infection in women should be obtained by catheter, voided specimens being worthless because of contamination from the external genitalia. Yet there is evidence that bladder catheterization is not without danger of actually producing urinary tract infection. Patients immobilized by poliomyelitis and other paralytic diseases are particularly prone to infections of the urinary tract. A method of obtaining urine specimens for culture by a clean voiding technique without resort to catheterization was investigated in order to detect and follow the course of urinary infections in a group of paralyzed poliomyelitis patients. Subjects for this study included 34 female patients with paralytic poliomyelitis admitted to the Poliomyelitis Respiratory Center and 8 female patients with no clinical findings indicative of urinary tract infection admitted to other hospital divisions. Twenty-one of the poliomyelitis patients were over 15 years of age, and 13 were younger. Virtually all were immobilized and recumbent for long periods, and all except 2 experienced respiratory failure necessitating mechanical respiratory aids.

Urine for study was collected by the voiding technique. The first specimen passed by the patient in the morning was discarded. The second specimen was preferred. With the patient in the dorsal

lithotomy position, the external genitalia were scrubbed thoroughly. Then the patient was encouraged to void, and the specimen was collected from the midportion of the urinary stream in a sterile container and immediately taken to the laboratory. It was either processed at once or stored in ice for not more than 3 hours. A catheterized specimen was obtained on the same day as the corresponding voided specimen, usually between 6 and 8 hours later.

Comparison of the paired samples collected from the poliomyelitis patients and from the controls according to the species and number of bacteria isolated revealed that satisfactory urine specimens for culture can be obtained by the voiding technique. When used in conjunction with colony counts or gram-stained smears of the urine, it is an adequate method of detecting significant bacteriuria in female patients. It is a valuable procedure for screening for urinary tract infection, especially in patients predisposed to urinary infection and in whom catheterization is almost certain to produce urinary infection. The risks inherent in bladder catheterization should not be neglected, and its use should be restricted to situations in which it is clearly indicated. To establish an accurate diagnosis of urinary tract infection, determination of the number of bacteria present in the urine is as important as their identification.

OTOLARYNGOLOGY

Carcinoma of the Larynx. G. E. Sheline and R. S. Stone. Ann. Otol. Rhin. & Laryng. **67**:1066-1072 (Dec.) 1958 [St. Louis].

At a recent symposium on carcinoma of the larynx, sponsored by the American Cancer Society, it was evident that considerable disagreement exists in regard to the relative indications for surgery and radiation therapy. At the University of California Hospital in San Francisco a close cooperation has existed between members of the departments of otolaryngology and radiation therapy, which has resulted in a policy by which all carcinomas of the larynx are seen jointly by the staffs of the two departments. In general, radiation therapy was given preference in all cases in which there was a reasonable possibility that irradiation would control the lesion. The present review analyzes the results in 124 patients with histologically verified squamous-cell carcinoma arising in the endolaryngeal mucosa and treated by primary x-ray therapy during the period from July, 1942, through June, 1952.

Ninety-six of the patients had primary lesions of the vocal cord. Of these 96 lesions, 58 were controlled by radiation therapy alone; 2 radiation failures were controlled by secondary laryngectomy. Of the 30 patients with lesions which could have been treated by cordectomy, 24 received radiation therapy and were living and symptom-free at 5 years after treatment. Twenty nine of the 43 cord lesions which would have required total laryngectomy were controlled by irradiation alone. Five of the 19 patients with cord carcinoma, too advanced for control by laryngectomy, were salvaged by radiation therapy. Only 4 of the 26 supraglottic carcinomas were controlled by irradiation, but apparently none of the patients with these lesions would have been good candidates for surgery. Neither of the 2 subglottic carcinomas responded to irradiation.

Deafness Following Maternal Rubella: Results of a Prospective Investigation. A. D. M. Jackson and L. Fisch. Lancet **2**:1241-1244 (Dec. 13) 1958 [London].

A national prospective inquiry into the effects of virus infections during pregnancy has recently been carried out by the Ministry of Health in Britain. During 1956-1957 a subsidiary investigation was undertaken on some of the children whose mothers had rubella during the first 18 weeks of pregnancy. The register of the national inquiry, which was compiled at the time of the mothers' pregnancy, included 79 surviving children from the counties of London and Middlesex whose mothers had rubella during the first 18 weeks of pregnancy. Fifty-seven of these children were still available for examination and constitute the rubella group. A control group, consisting of 57 children whose mothers had no infection during pregnancy, was also examined. The examination team consisted of a pediatrician, an otologist, an educational psychologist, and an audiology technician with experience in testing young children.

Reliable audiograms were obtained in all but 7 of the 114 children examined, and in these 7 the voice tests were considered adequate for the diagnosis of deafness to be confirmed or excluded. Fourteen of the 57 children whose mothers had had rubella during early gestation had congenital deafness. Such a diagnosis was made if the audiogram showed a hearing loss of 20 db. or more in at least 2 adjacent frequencies, or a loss of 30 db. or more in a single frequency. In 2 of the 7 children from whom reliable audiograms could not be obtained, a diagnosis of severe bilateral deafness was made

on the results of other hearing tests. The remaining 5 children were considered to have normal hearing, but, in the absence of reliable audiograms, the possibility of minor degrees of hearing loss could not be excluded. In 5 of the 14 children the deafness was unilateral.

Since Gregg's original report on the effects of rubella during pregnancy in 1941, the early retrospective studies suggested that the incidence of congenital defect, including deafness, was very high. Later prospective investigations showed it as much lower. The authors believe that theirs is the first investigation to include detailed hearing tests with audiograms on a group of children from a prospective series. The group is to some extent selected, because it includes only live-born children from the national inquiry who survived to the age of 4 years and lived in the London area. The fact that 9 out of 14 cases of congenital deafness had not been detected by the age of 4 years indicates the importance of detailed hearing tests, including audiograms, in the diagnosis of deafness caused by rubella during gestation.

THERAPEUTICS

On the Use of Liver Extracts Regulating the Action of the Heart in Surgical Patients. C. Uggeri. Minerva med. 49:3928-3933 (Oct. 20) 1958 (In Italian) [Turin, Italy].

The author reports on his experience with Cortunon, an Italian proprietary liver-extract preparation which has a regulatory effect on the action of the heart. The extract was given to 174 surgical patients—to 83 before the operation and to 91 after the operation. The 83 patients who received the drug before the operation were given 3 intramuscular injections of 2 cc. per day for 2 to 4 days, followed by 2 injections per day, one in the morning and the other in the evening, for the remaining period preceding the operation, usually from 4 to 8 days. The treatment was resumed by mouth soon after the operation in half of these patients and was continued for a period of 5 to 10 days. Patients whose condition was serious received a beginning dose of 12 cc. per day, given in 3 injections, and a continuing dose of 6 to 8 cc. per day.

Liver-extract treatment in most of the patients was combined with analeptic or cardiotonic treatment and was well tolerated generally and locally. In 9 patients with exophthalmic goiter the drug was combined with other substances, such as iodine, sedatives, and vitamins. The heart condition of 6 of these patients improved within 2 to 4 days; their pulse rate diminished 20 to 35 beats per minute. In one patient the pulse rate which was 130 per minute was reduced to 80 per minute after 6 days of treatment with 6 cc. of Cortunon per day; the subjective symptoms disappeared. Three patients, who had been under medical treatment for several years but with poor results, derived no benefit from the liver-extract preparation until after a subtotal thyroidectomy. Poor results were obtained in 3 patients with essential hypertension, and there was no effect on the pulse rate of 4 patients with valvular lesions. Subjective symptoms, though, disappeared in 6 of 7 patients with coronary disease; in 1 patient with atrioventricular block and in 2 patients with early auricular fibrillation, the administration of Cortunon had a permanent beneficial effect.

Anticoagulants in Therapy of Arteriosclerosis. O. Castro Bianchino. Tórax 7:77-87 (March) 1958 (In Spanish) [Montevideo, Uruguay].

Eighty-three patients with arteriosclerosis were treated with anticoagulants during the past 3 years at the Puriel Semiologic Clinic in Montevideo. Before the treatment cholesterolemia was normal in 52 out of 66 patients and was increased in 14. The total lipids were normal in 35 out of 74 patients and were increased in 39. The lipidograms showed pathological tracings for 68 out of 83 patients and were normal for 15. The presence of hemorrhagic diseases and of diseases which are frequently complicated by hemorrhages was regarded as contraindication for anticoagulant treatment. Fourteen patients with myocardial or pulmonary infarction were treated with Tromexan (a coumarin derivative). The drug was given by mouth in an initial dosage which varied between 600 and 900 mg. divided into 2 or 3 fractional doses. The maintenance doses were regulated by the results of periodic determinations of the blood prothrombin time. Fourteen patients with cerebral or coronary arteriosclerosis or with arteriosclerosis of the legs had intravenous injections of a heparin solution, each injection containing 7,500 I. U. of the drug in 1.5 cc. The injections were given 3 times a week for 2 or 3 consecutive months. The remaining 55 patients were excluded from the study owing to their irregularity in reporting for consultation.

Either treatment was aimed at modifying the metabolism of lipids and the humoral changes which are responsible for pathological abnormalities in the wall of the arteries. Tromexan had no effect on the metabolism of lipids. Heparin, on the other hand, regulated the metabolism of lipids in the 14 patients to whom it was administered. The total lipids were increased in 10 patients, and the lipidogram tracings showed considerable improvement for 9. Great improvement from heparin treat-

ment was obtained in 7 patients with anginal symptoms from coronary arteriosclerosis and in 4 patients with arteriopathy of the legs, with painful intermittent claudication. The satisfactory results have been maintained in all 11 patients for more than 3 months since discontinuation of the treatment. In the 3 patients with cerebral arteriosclerosis, though, the results of heparin treatment were mediocre. The tolerance of the 11 patients for heparin was perfect; none of them exhibited anaphylactic reactions. Since the treatment is expensive, it should be given only when (1) the lipidograms are characteristic of the disease, (2) there is a deficit in the amount of heparin in the blood, and (3) there are anginal symptoms or painful claudication of the legs.

Therapeutical Results as Obtained with Plasma Gamma Globulins of Human Origin: A Survey Covering 6,602 Cases: I. Main Indications for Their Use in Infectious Diseases. J. P. Soulier, M. Badillet and F. Herzog. Presse méd. **66**:1881-1884 (Nov. 29) 1958 (In French) [Paris].

The authors give the results of a survey covering 6,602 cases of measles, whooping cough, rubella, mumps, smallpox vaccination complications, and smallpox, which were treated by the administration of plasma gamma globulins of human origin. The preparation was also used to prevent measles in 3,702 persons. The authors present results by groups in towns and in collectives. In the case of measles, injection of a solution of gamma globulins was generally practiced in the first half of the supposed incubation period of the disease. Complete protection against measles was provided for 878 persons out of 1,201 in the town group (73.2%). In 323 persons protection was not complete, and measles resulted, usually in an attenuated form; 125 of these patients had been exposed to prolonged contagion. In 3 of the failures titers of antibodies were insufficient, and in 19 of them the injection was given too late. Prophylaxis of measles in infants exposed to contagion was justified. The quality of attenuation was in direct proportion to the date of injection of the gamma globulin solution. In the group of collectives there were 3 categories: nurseries with healthy children; homes for children of different ages, frequently with physical weaknesses; and hospitals for sick children of different ages. A total of 2,501 children received injections; of this number 2,280 were completely protected against measles by the gamma globulin solution, but 182 had mild cases of the disease and 39 developed severe cases. Eighty-one patients who were given the preparation as a curative treatment of measles showed satisfactory results. In 12 patients measles was complicated by encephalitis, but 11 of them were completely cured.

Curative treatment of whooping cough with a solution of gamma globulins was beneficial for 150 patients treated at the Hospital for Sick Children in Paris. Therapeutic results were excellent in 144 patients, were average in 44, and were absent in 38. Preventive treatment of whooping cough resulted in complete protection of 360 persons out of 437 attempts. A survey of 349 patients was conducted essentially to define the preventive action of gamma globulin therapy on rubella in pregnant women and on congenital malformations in their children. Of 315 pregnant women, the majority of whom had been closely exposed to rubella, 312 were completely protected by the injection. The condition of the infant was described in 229 cases. Only one defect might possibly be attributed to rubella; this was a case of mental retardation, and it may not have been caused by the disease, because the exposure took place during the 6th month of pregnancy. Eight pregnant women with rubella received the gamma globulin solution curatively. The infant of one patient had not yet been born; the other pregnancies resulted in one miscarriage, one infant who died soon after birth, one infant with a light psychomotor retardation, and 4 normal children.

When the gamma globulin injections were used to prevent mumps, 92 out of 104 persons were completely protected, 10 contracted the mild form, and 2 developed severe cases. Thirty-six patients with mumps were treated with the preparation in an effort to shorten the course of the disease and to prevent complications. Results were good, particularly in orchitis parotidea which was cured in 3 or 4 days. Thirty-eight persons who had the gamma globulin treatment successfully escaped the complications of antismallpox vaccination. The therapeutic effect of these injections on 34 patients who developed such complications was good, with a rapid reduction in general signs and a fall in fever within a few hours. Sixty-eight persons who had been exposed to smallpox received the gamma globulin preparation, and all except 12 who had slight fever or benign smallpox escaped the disease. A cure with gamma globulin treatment was effected in one case of smallpox with complications.

Observations on Antibiotics in the Treatment of Hepatic Coma and on Factors Contributing to Prognosis. J. M. Stormont, J. E. Mackie and C. S. Davidson. New England J. Med. **259**:1145-1150 (Dec. 11) 1958 [Boston].

The observation that urea-splitting bacteria in the colon were a significant factor in ammonia production and the demonstration of decreased portal-vein ammonia after the administration of antibiotics suggested that antibiotics should be of value in the treatment of hepatic coma. The combination of chlortetracycline with protein depriva-

tion was shown to produce significant improvement in many patients with hepatic coma. Dietary protein has, however, been shown to be essential for adequate liver function in human subjects and animals. Neomycin administration to patients with chronic hepatic coma will allow additions of protein in amounts otherwise not tolerable. Since patients with cirrhosis may be in nitrogen balance with 30 to 50 Gm. of dietary protein, patients with hepatic coma at the Boston City Hospital have recently been treated with neomycin or paromomycin and protein withdrawal for 2 to 4 days; this was followed by administration of about 30 Gm. of dietary protein daily while antibiotics and other therapeutic measures were continued, the protein intake subsequently being increased as improvement occurred. In the last 2 years the authors studied 68 patients in hepatic coma or precoma. Sixty patients were considered to have cirrhosis of the alcoholic type, and 5 had "postnecrotic" cirrhosis, although a history of alcoholism was present in 2 of these. Two patients with hemochromatosis and one with metastatic carcinoma involving the liver were also included.

Seventy episodes of hepatic coma or impending coma were observed in the 68 patients, with recovery in 27 (39%). Twelve patients received chlortetracycline. Excluding these, there were 58 episodes in 56 patients, with recovery in 23 (40%) and improvement in 41 (71%), usually within 48 hours; of these 58 episodes, the patients in 34 were treated with paromomycin, resulting in 14 recoveries (41%), and in 24 with neomycin, resulting in 9 recoveries (38%). Thus, there was essentially no difference among the various antibiotics used in conjunction with readministration of protein. Comparison with 35 patients treated with complete protein withdrawal and chlortetracycline in the same hospital during the previous year also revealed no important difference in improvement and recovery. The majority of fatalities were related to potentially correctable complications, such as hemorrhage and infection. Liver failure was also an important cause of death, and prognosis was adversely affected by elevated serum bilirubin or electrolyte abnormalities. No evidence of neomycin or paromomycin toxicity was encountered, and severe diarrhea was not a problem with the doses used in this regimen.

Production of Impending Hepatic Coma by Chlorothiazide and Its Prevention by Antibiotics. J. E. Mackie, J. M. Stormont, R. M. Hollister and C. S. Davidson. New England J. Med. **259**:1151-1156 (Dec. 11) 1958 [Boston].

Development of impending hepatic coma, characterized by confusion, drowsiness, and flapping tremor, has been described previously in patients with cirrhosis given nitrogenous substances by mouth—ammonium cation-exchange resins, ammonium salts, urea, methionine, and increments in dietary protein. It has also been reported in patients given a carbonic anhydrase inhibitor, acetazolamide. The authors here report the production of impending hepatic coma in alcoholic patients with cirrhosis and ascites given chlorothiazide, a nonmercurial diuretic agent. Chlorothiazide, administered to 5 alcoholic patients with cirrhosis and ascites, was observed to produce impending hepatic coma in 3 of these patients. This was associated with increased arterial ammonia concentration, increased sodium and potassium excretion, and a fall in serum potassium concentration. Impending hepatic coma was prevented by the concurrent administration of broad-spectrum, nonabsorbable antibiotics, and the oral administration of potassium chloride supplements prevented hypokalemia. The authors conclude that chlorothiazide is a useful diuretic agent in some patients with cirrhosis and ascites, but these patients must be carefully observed for the development of impending hepatic coma and hypokalemia. Potassium chloride supplements may be necessary.

PATHOLOGY

Malignant Cells in Peripheral Blood. J. C. Pruitt, A. W. Hillberg and R. F. Kaiser. New England J. Med. **259**:1161-1164 (Dec. 11) 1958 [Boston].

This report is concerned with the study of results obtained by the use of a new method by which it is possible to examine quantitatively up to 20 ml. of peripheral blood for the presence of malignant tumor cells. In cooperation with the health office of Washington County, Maryland, and the private physicians of Hagerstown, Md., 20-ml. specimens of peripheral blood were obtained from a vein in the antecubital fossa of patients with and without cancer. The usual technique of venipuncture was used, but the syringe contained approximately 50 mg. of Lipo-Hepin to prevent coagulation. The blood was collected in sterile tubes and refrigerated for brief periods, permitting transport to the central laboratory.

The procedure for processing the blood was that described by Malmgren and associates (*J. Nat. Cancer Inst.* **20**:1203, 1958). The procedure involves the addition of streptolysin O as hemolysin and leukocidin followed by passage of the resultant material through Millipore filters. Five or six filters are required for each specimen. The filters are removed after filtration from the special funnel apparatus and stained by the Papanicolaou technique. After staining, each entire filter is mounted on a glass slide and permanently sealed with permount and a cover slip. The slides are then ready for microscopic examination. Three hundred blood specimens, obtained from 100 patients with cancer

and from 200 presumably well people, were studied. Examination revealed that cytologically malignant cells were identifiable in 39% of patients with cancer, and suspicious cells were present in an additional 12%. In the control group of 200 persons, cells that were considered to be cytologically malignant were found in only one (or 0.5%).

It seems likely that malignant squamous cells exfoliate into the blood at least as often as cells from adenocarcinomas. Sarcomas exfoliate cells into the blood with about the same regularity as carcinomas. Melanoma cells were found in the peripheral blood of 2 patients out of the 3 examined. These melanomas were not advanced, and the patient whose specimen was negative had been treated by total excisional biopsy 3 days before the specimen was obtained. It seems that one has about the same chance of identifying malignant cells in the peripheral blood in patients whose disease is local only but no treatment has yet been instituted as in patients whose disease has spread from its site of origin but treatment has been obtained. The reasons for this are not entirely clear, except that most often the spread of the lesion is to the lymph nodes, and these nodes may act as filters. A statistically significant analysis of the relation of the site of origin of the tumor to the presence of malignant cells in the peripheral blood proved impossible, but the biological activity of the tumor seems to be of importance. Malignant cells are not present in enough volume to justify examination of peripheral blood to make a primary diagnosis of cancer except in suspected cases that have eluded diagnosis by other means. Further evaluation of the method is required. It may be of value to follow patients after operation to indicate the presence of unsuspected metastases.

Analysis of Lipids of the Arterial Wall. C. J. F. Böttcher, J. G. Keppler, C. C. ter Haar Romeny-Wachter and others. Lancet **2**:1207-1209 (Dec. 6) 1958 [London].

The authors carried out a detailed analysis of the lipids extracted from 22 single human aortas in different stages of atherosclerosis, which were obtained from autopsies performed at the laboratory of pathological anatomy of the University Hospital in Leiden, The Netherlands. Phospholipids, free fatty acids, sterol esters, glycerol esters, and free sterols were extracted from these aortas. The composition of the fatty acid mixtures from 4 of these 5 fractions were analyzed by gas chromatography. The results of these studies did not confirm the hypothesis that the deposition of saturated cholesterol esters is a characteristic feature of atherosclerosis. On the contrary, the proportion of saturated sterol esters fell as the severity of atherosclerosis increased, as also did the proportion of saturated phospholipids. The degree of saturation of triglycerides bore little relation to the degree of atherosclerosis. The authors decided to continue their analyses, paying special attention to the ratio between nonessential and essential unsaturated fatty acids deposited in the aorta, and a more detailed account will be published soon.

Experimental Production of Carcinoma with Tobacco Products: V. Carcinoma Induction in Mice with Cigar, Pipe, and All-Tobacco Cigarette Tar. A. B. Croninger, E. A. Graham and E. L. Wynder. Cancer Res. **18**:1263-1271 (Dec.) 1958 [Chicago].

The authors previously published results of the experimental production of carcinoma of the skin in mice after application of cigarette tar condensate in 3 strains of mice, as well as in rabbits. The present study is concerned with comparing the biological activity of different types of tobacco products, such as cigars, pipes, and all-tobacco cigarettes. The smoking machine and the manner in which cigarettes were smoked and tars prepared for use were described in previous publications. A popular brand of cigars was puffed 3 times a minute, pulling a 50-ml. puff over a period of 4 seconds. This increase in volume and length of puff was necessary to keep the cigars lit and to give an adequate draw. The smoking time averaged 26 minutes. All-tobacco cigarettes were prepared by wrapping cigarette tobacco in tobacco leaf. These special cigarettes were smoked under the same conditions as standard cigarettes, but, owing to the waxy tobacco outer wrapping, they were smoked more slowly than the latter, averaging 16½ minutes per cigarette.

The most important finding of this study is that all types of tobacco smoke condensate tested have substantial carcinogenic activity. This observation is in line with human epidemiologic data which show a relationship between all types of tobacco smoke and cancer of the respiratory tract, that of cigarettes mainly for the lung and that of cigars and pipes primarily for the oral cavity. The highest percentage of both papillomas and cancers was found in the group of Swiss mice painted with nicotine-free pipe and cigar tars. This indicates a somewhat higher degree of carcinogenic activity for cigar and pipe tars than for cigarette tar and a somewhat less activity for all-tobacco cigarette tar compared with standard cigarette tar. Some of the differences could be a result of differences in biological variation. A comparison of whole tobacco tar with diluted tobacco tar suggests that dilution of tar accelerates tumor formation, apparently as a consequence of increased absorption of tobacco carcinogens. A comparison of the carcinogenic activity of freshly prepared tar with that of "old" cigarette tar showed no differences in activity. Present data reemphasize the viewpoint that tobacco carcinogens are formed during the process of combustion of tobacco and that the amount of tobacco

carcinogens formed depends on the temperature reached and the completeness with which the combustion process occurs. Preventive measures directed toward reducing tobacco carcinogens must apply to all tobacco products.

Observations on Aberrant Renal Arteries Curving Around and Compressing the Renal Vein: Possible Relationship to Orthostatic Proteinuria and to Orthostatic Hypertension. H. Nathan. Circulation **18**:1131-1134 (Dec.) 1958 [New York].

On the dissection of 400 renal pedicles obtained from 200 dissecting-room cadavers in Philadelphia and Jerusalem, the author found in 7 cases (3.5%) an aberrant inferior polar renal artery, curving around the normal renal vein. Six of these aberrant vessels were on the left side, and one on the right. The polar renal artery originated from the aorta below the level of the corresponding renal vein, and proceeded upward and laterally behind the vein. At the upper border of the vein, the artery curved downward and descended in front of the vein, to reach the kidney near its lower pole. The artery thus described an arch over the renal vein. In all instances the artery was intimately related to the renal vein, which appeared constricted and angulated under the arch of the artery. This kind of aberrant artery could be the cause of compression of the renal vein, particularly in the erect posture. The possible consequences of such compression are discussed with special reference to orthostatic proteinuria. The possibility also is considered of the aberrant artery being partially compressed by the renal vein, again particularly in the erect posture. Should this occur, an "intermittent Goldblatt mechanism" might be established, which would offer an explanation for the causation of some cases of orthostatic or postural hypertension described in the literature.

BIOCHEMISTRY

Critical Evaluation of the Precipitation Test for Systemic Lupus Erythematosus. L. E. Böttiger. J. Lab. & Clin. Med. **52**:909-911 (Dec.) 1958 [St. Louis].

The precipitation test with which Böttiger is concerned was described by Jones and Thompson in THE JOURNAL, March 22, 1958, page 1424. The test is carried out by adding a 12% solution of *p*-toluenesulfonic acid in glacial acetic acid to serum. The authors claimed the test to be specific for systemic lupus erythematosus and stated that they had found very few false positives. These false-positive reactions were found in cases of hepatitis, in disseminated coccidioidomycosis, and in 2 cases of fulminating multiple myeloma. It is well known that an increase of the gamma globulin fraction in the serum is often found in systemic lupus erythematosus. This also is the case in diseases that give false-positive reaction. To test the hypothesis that the precipitation test is a nonspecific reaction, 158 serum samples were examined. All had been sent to the department of clinical biochemistry for various routine analyses from different departments of the Karolinska Hospital in Stockholm. Results of the examination of the 158 serums seemed to indicate that the test was not specific for systemic lupus erythematosus but dependent on the gamma globulin content of the serum.

Absorption of Vitamin B_{12} in Pernicious Anemia: Defective Absorption Induced by Prolonged Oral Treatment. M. Schwartz, P. Lous and E. Meulengracht. Lancet **2**:1200-1204 (Dec. 6) 1958 [London].

The authors studied vitamin B_{12} absorption in patients with pernicious anemia, both treated and untreated. Without intrinsic factor the urinary excretion of radiocobalt (Co^{60}) vitamin B_{12} in 17 untreated patients with pernicious anemia varied between zero and 4.4% as compared with normal values varying between 10 and 40%. When Co^{60} vitamin B_{12} was administered together with 100 mg. of hog pyloric mucosa, the excretion in all the patients attained normal levels, with values ranging from 12.4 to 29.5%. All these patients with untreated pernicious anemia had some, although very slight, spontaneous intrinsic factor activity, the average excretion being 2.2% without supplementary intrinsic factor. Sixteen patients with pernicious anemia treated solely with new preparations of vitamin B_{12} combined with hog pyloric mucosa, administered orally for periods varying from 3 months to 4 years, were examined in the same manner without intrinsic factor and with 100 mg. of hog pyloric mucosa. Only 5 patients showed a normal absorption of vitamin B_{12}, and the remaining 11 showed blockage of absorption of vitamin B_{12}. Vitamin B_{12} absorption tests also were performed on 10 patients with pernicious anemia treated solely with the old-type preparations of crude stomach (pylorus) for several years. Of the 10 patients, 2 showed subnormal absorption values with 100 mg. of hog pyloric mucosa; but these patients, despite the extremely long period of therapy, absorbed vitamin B_{12} excellently, in sharp contrast to patients treated with combination preparations for quite brief periods. Most of the patients who have had pernicious anemia for a long time have lost the last spontaneous intrinsic factor activity, the average excretion of vitamin B_{12} without supplied intrinsic factor being 0.6%, as compared with 2.2% in the untreated patients.

The blockage of absorption of vitamin B_{12} caused by oral treatment of pernicious anemia with combined preparations of vitamin B_{12} and hog pyloric

mucosa, demonstrated previously, was confirmed. Such blockage is very common, and it often occurs after treatment for a few months. Patients treated with preparations of crude pylorus either develop this blockage not at all or to a negligible extent. The blockage is related to hog pyloric mucosa. Vitamin B_{12} bound to this substance is poorly absorbed despite the presence of active human intrinsic factor. Alterations in the intestinal flora do not appear to explain the blockage. The blockage is not present in absorption tests with homologous intrinsic factor or with intrinsic factor from another species (rat). This observation supports significantly the hypothesis that blockage is an immunity phenomenon, the intrinsic factor being to some extent species-specific.

PUBLIC HEALTH

Effectiveness of Influenza Vaccines During an Epidemic of Asian Influenza. B. F. Gundelfinger, W. T. Stille and J. A. Bell. New England J. Med. **259**:1005-1009 (Nov. 20) 1958 [Boston].

An epidemic of respiratory illness, associated with Asian influenza, occurred in the early fall of 1957 at the United States Naval Training Center, Great Lakes, Ill. Of 3,355 Navy recruits who arrived at Great Lakes between Aug. 7 and Sept. 18, 1957, about 30% were given a 1-cc. subcutaneous inoculation of monovalent influenza-virus vaccine (A/Japan/305-57) reported by the manufacturer to contain 200 chick-cell-agglutinating (CCA) units per cubic centimeter (vaccine A). Another group (about 30%) were given a 1-cc. subcutaneous inoculation of polyvalent influenza vaccine containing 250 CCA units, each of Formalin-inactivated A/Swine, A'/FM1, and B/GL/1739-54 viruses (vaccine B). The remainder of the recruits (about 40%) were given an inoculation of either a trivalent adenovirus vaccine or a placebo inoculation and served as controls. Of 964 recruits in whom febrile respiratory disease occurred during the study period from Aug. 25 to Nov. 9, 1957, 152 were inoculated with vaccine A, 299 received vaccine B, and 513 were in the control group. This gives an attack rate of 23.5 per 1,000 per week in the vaccine A group, 49.7 per 1,000 per week in the vaccine B group, and 58.9 per 1,000 per week in the control group. During the epidemic an 83 to 90% reduction in febrile respiratory illness was associated with prior inoculation with a monovalent Asian-influenza vaccine containing only 200 CCA units of A/Japan/305-57-strain virus. A similar 21 to 46% reduction was associated with prior inoculation with the polyvalent influenza vaccine not containing the Asian strain. Although a marked protective effect was noted as early as 10 days after inoculation, a slight beneficial result was noted before that time. No untoward reactions to the vaccine were observed. It is concluded that the Asian influenza vaccine was highly efficacious under the conditions of use at Great Lakes in the fall season of 1957.

Effect of Eradicating Brucellosis in Cattle on Incidence of Human Cases. J. R. Held, H. Bauer and R. L. West. Pub. Health. Rep. **73**:1096-1100 (Dec.) 1958 [Washington, D. C.].

Brucellosis was first reported in humans in Minnesota in 1927, and there was a general trend toward an increasing number of cases until 1946. Since 1946 the trend has been downward, for whereas the case rate per 100,000 population was 13.84 in 1946, it was 1.94 in 1956. An awareness of the presence of brucellosis in the state was needed before the majority of cases could be diagnosed. In 1927 serologic and bacteriological services were introduced into the laboratories of the Minnesota Department of Health to aid in the diagnosis of brucellosis. These services have been used increasingly by practicing physicians since that time. The only cases counted by the Minnesota Department of Health are those confirmed by an agglutination test with a titer of at least 1:80, accompanied by clinical symptoms suggestive of brucellosis, or confirmed by isolation of the Brucella organisms from blood cultures.

This paper is particularly concerned with the effect of the area certification program on the number of human cases of brucellosis. In 1939 the Minnesota Legislature enacted a law authorizing the State Livestock Sanitary Board to control and eradicate brucellosis in cattle by means of an area plan. Under this plan all cattle owners in a specified area are required to participate in a testing program. The law also provides for the slaughter or isolation of all cattle reacting to tests and regulates the importation of any cattle into the area according to whether the animals, or herds from which they originate, are infected or not. By 1956 all the counties in the state were operating under this plan. Coincident with progress in the eradication of brucellosis in cattle, there has been a significant reduction in the number of human cases. Since 1940, when the first counties were certified, the case rate has been 3.12 times greater in noncertified than in certified counties.

Other factors undoubtedly affecting the number of human cases of brucellosis in Minnesota are the number of cattle in the state. From 1927 to 1948, when the number of cattle increased or decreased, there was a corresponding increase or decrease in the number of human cases of brucellosis. But from 1950 to 1956 the number of human cases declined markedly in spite of a high increase in the cattle population. This change in trend results from the elimination of some sources of human infection by the acceleration of the program of eradicating the disease in cattle.

BOOK REVIEWS

The ABO Blood Groups: Comprehensive Tables and Maps of World Distribution. By A. E. Mourant, M.A., D.Phil., D.M., Director, Medical Research Council Blood Group Reference Laboratory, Lister Institute of Preventive Medicine, London, Ada C. Kopeć, D.és Sc., Statistician, Nuffield Blood Group Centre, London, and Kazimiera Domaniewska-Sobczak, M.A., A.L.A., Librarian, Nuffield Blood Group Centre. Occasional publication no. 13 of Royal Anthropological Institute. Cloth. $8.50. Pp. 276, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada. 1958.

The authors of the monograph have made a useful contribution to physical anthropology by compiling and tabulating the results of the studies on the distribution of the A-B-O groups and the subgroups of A throughout the world. For all large populations, moreover, the frequencies of the blood group genes have been calculated and tabulated. A debt of gratitude is due the authors for having undertaken the Herculean task of culling the vast literature, classifying the data, computing gene frequencies, and publishing all this information in a single volume.

Recent Advances in Pædiatrics. Edited by Douglas Gairdner, M.A., D.M., F.R.C.P., Pædiatrician to Addenbrooke's Hospital, Cambridge. Second edition. Cloth. $9.50. Pp. 378, with 82 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England.

This edition follows its predecessor by four years with a compendium of 13 articles covering those pediatric fields in which it is considered that significant progress in understanding or treatment has recently been made. The contributing authors are English with the exception of three American writers of two chapters. The following subjects are covered: changes in circulation at birth and the effects of anoxia, hematology of infancy, jaundice in the newborn, physical growth, hypothyroidism, spina bifida cystica, hydrocephalus of infancy, the nephrotic syndrome, tuberculosis, rheumatic fever, the deaf child, and pyogenic osteitis. Each of these small monographs gives either a complete résumé of the present investigational or therapeutic understanding in its field or a survey of newer approaches made, as in the case of childhood deafness. The chapters on hematology, jaundice of the newborn, and rheumatic fever are the most extensive and are full of practical, useful information. The section on tuberculosis is informative as to the control of this disease and the influence of the newer drugs and hormones on its course. Some of the articles are based primarily on the author's experience while others quote extensively from the current literature. Every chapter has a good up-to-date bibliography. Thus each section provides an excellent orientation and survey of a field of pediatrics in which significant progress in treatment or knowledge has been made. The British concepts do not differ from those held in the United States. This book is recommended as a better than usual source of information on its 13 subjects for any physician concerned with these problems in children.

Streptomycin and Dihydrostreptomycin. By Louis Weinstein, Ph.D., M.D., Professor of Medicine, Tufts University School of Medicine, Boston, and N. Joel Ehrenkranz, M.D., Assistant Professor of Medicine, University of Miami School of Medicine, Coral Gables, Florida. Foreword by Chester S. Keefer, M.D. Antibiotics monographs no. 10. Under editorial direction of Henry Welch, Ph.D. and Félix Martí-Ibáñez, M.D. Cloth. $4. Pp. 116, with 13 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22. Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book provides a clear and reasonably complete exposition of the history, properties, methods of susceptibility-testing and assay, bacterial resistance and synergism with other antimicrobials, pharmacology, untoward reactions, and uses in various types of clinical infections, including application in combination with other antibiotics, of streptomycin and dihydrostreptomycin. A brief final chapter describes the use of streptomycin in the isolation and culture of viruses. Although the authors have not attempted to review all previously reported studies, the book takes into account most of the important published papers on the streptomycins. It is unfortunate that no reference was made to the study reported by Wier and co-workers (*Dis. Chest* 30:628-632 [Dec.] 1956) which revealed that, from the standpoint of hearing impairment only, therapy with the combination of streptomycin-dihydrostreptomycin (Streptoduocin) may be more hazardous than with streptomycin alone. The bibliography provided is extensive and is annotated in the text. A subject index included at the end appears to be carefully compiled. This book should be welcomed by all clinicians as well as laboratory investigators who have a special interest in antibiotics.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

WEIGHT GAIN AFTER CESSATION OF SMOKING

To the Editor:—*Many persons who stop smoking quickly gain weight. In most of them this is undoubtedly due to an improved appetite with consequent increase in calorie consumption, but some who have "kicked the habit" stoutly maintain that they are gaining weight in spite of the fact that they have not increased either food or beverage consumption. Is there any metabolic change that might account for some of this weight gain?*

John Trapnell, M.D., Philadelphia.

Answer.—Weight gain after cessation of smoking, just as true weight gain under any circumstances, must be due to an excess of calorie intake over calorie expenditure. The insidious increase of calories is effected by two significant factors. Smoking may inhibit gastric motility for 15 to 60 minutes; consequently, in most chronic smokers hunger and appetite are depressed. Psychic restlessness, previously satisfied by smoking, is now appeased by the substitution of food. As in most obese persons, minor nibbling and between-meal snacks may add up to an astonishing number of calories. The pharmacological effects of nicotine are complex. An immediate stimulating action on the autonomic nervous system, the adrenal medulla, and vasomotor cortex occurs, which results in an increase in heart rate, cardiac output, and respiratory rate and elevation in blood pressure. These may, in turn, cause acceleration of metabolic processes, but this initial action is followed by depression of the same systems so that one must assume that the effect is the summation of these two phases. It must therefore be concluded that little alteration in metabolic processes occurs after cessation of smoking.

SKIN DIVING AND POLYCYTHEMIA VERA

To the Editor:—*Is there a relationship between skin diving and true polycythemia vera? In a 35-year-old man with a hemoglobin level of 21 Gm.%, should further diving be restricted?*

Richard O. Bagley, M.D., Richmond, Calif.

Answer.—Some distinction might be made between scuba diving (self-contained underwater breathing apparatus) and snorkel diving. The former does not involve breath-holding, but the latter does to some extent. Snorkel diving might therefore be expected to induce an adaptive polycythemia and intensify symptoms, if any, of an already existing polycythemia. This is purely theoretical, however, for no case has been reported of an adaptation of this sort or any deaths or sickness in skin divers with symptoms (thrombosis or hemorrhage) suggesting polycythemia as a contributory cause. There is no record of actual experience that would justify restricting this man's activities in this direction. A remarkable article by Auerback and associates (*Pediatrics* **21**:54, 1958) includes mention of a 12-year-old boy who had hemoglobin levels as high as 24 Gm.% with no symptoms other than "pink-eye." These authors believed that the presence or absence of troublesome symptoms should determine whether anything should be done in the way of limiting activities or starting treatment.

MONGOLISM

To the Editor:—*An article in a Spanish medical journal discussed the treatment of Mongolism with androgens, with favorable results. Is dehydroepiandrosterone available in the United States? Please comment also on powdered calf pituitary extract in the treatment of Mongolism.*

O. L. Frank, M.D., Maquoketa, Iowa.

Answer.—Hormonal treatment of Mongolism was first advocated in the United States several years ago. The regimen advocated consisted of the oral administration of pituitary substance from the immature animal (calf), on the premise that the pituitary of the immature and adult animal differ in growth-stimulating ability, plus thyroid substance as a mordant. Several aspects of this treatment may be viewed with concern. The cause of Mongolism remains unknown. Although histological changes in the pituitaries and thyroids of affected persons have been demonstrated, there is as yet no evidence for hypofunction of these or any other endocrine systems in Mongolism per se. Several studies have shown normal thyroid function in patients with Mongolism. Bovine growth hormone has not proved effective in the treatment of growth failure in man. Animal studies have demonstrated no difference in the growth-stimulating ability of the immature and adult pituitary, and growth hormone is not effective by the oral route. Reports of this form of therapy have not shown significant improvement in Mongolism. Clin-

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ical and biochemical evidence of hypothyroidism has been noted in some such persons and evidence of hyperthyroidism in a very few. Here, appropriate therapy may be directed toward the thyroid disturbance, but it leaves the Mongoloid state unchanged. There is no evidence of androgen deficiency in persons with Mongolism and, therefore, no rationale for its administration. There are no known indications for the clinical use of dehydroepiandrosterone. It is commercially available in the United States for laboratory use.

METHANE IN WATER SUPPLY

To the Editor:—*A newly driven well, 380 ft. deep, emits what appears to be natural gas. Does this admixture of gas render the water hazardous for household use? Should the water be submitted for chemical analysis and, if so, to whom?*

Charles H. Kosmaler, M.D., Elmira, N. Y.

Answer.—If the gas is methane, as it probably is, the water is dangerous to use because of the explosion hazard. A method of collecting and analyzing water samples for methane is given by Buswell and Larson (*J. Am. Water Works A.* **29**:1978, 1937). The state or local health department can give advice on this problem. Carbon dioxide is a more common gas in ground waters. Since carbon dioxide is removed by passage through lime water or sodium hydroxide, a qualitative test can be done to determine whether the gas in question is carbon dioxide.

CHRONIC OTITIS MEDIA

To the Editor:—*A 15-year-old boy has had chronic otitis media for several years. The drainage is purulent and often sanguineous. Examination revealed an old perforation, now barely visible, with chronic inflammation and drainage over the canal and drum. Roentgenograms taken in July, 1957, and October, 1958, showed no change, no cholesteatoma, and apparently normal mastoids. Culture revealed Staphylococcus pyogenes var. aureus sensitive to chloramphenicol, streptomycin, nitrofurazone, neomycin, and erythromycin. Chloramphenicol by mouth and in ear drops was tried for one week with little change. Cortisone had been tried previously with transient success and later with no success. What treatment should be used?* *M.D., Washington.*

Answer.—This is a chronic suppurative otitis media. The information furnished is not sufficient for a specific answer. Regarding the roentgenograms, which were said to show no cholesteatoma and apparently normal mastoids, such films frequently do not give definitive information. Cholesteatoma in the attic, for example, may not show up on a roentgenogram except in special films which have been carefully made. The culture in a chronic condition is frequently not significant, since it varies from time to time. The most essential information needed to understand the pathological process in this case is the finding on otoscopic examination. For example, a perforation in the pars flaccida of the tympanic membrane or along the upper periphery of the drum has quite a different significance from a central perforation in the membrane proper. A history that includes such factors as recurring upper respiratory infections, allergic episodes, and obstruction to nasal breathing is significant. Without such information it is not possible to give an intelligent opinion as to how such a condition should be treated.

TRIPLE VACCINE

To the Editor:—*Is triple vaccine (pertussis, tetanus, and diphtheria antigens) to be preferred to double vaccine (tetanus and diphtheria only) when immunizing children of grade school age?*

C. W. Truesdale, M.D., Glencoe, Minn.

Answer.—There should be no doubt that it is preferable to give the triple antigens rather than tetanus and diphtheria alone when conducting a campaign of primary immunizations. The pertussis vaccine might be omitted if a child was known to have had whooping cough. Pertussis can be a serious disease in young children as well as in infants.

COMPOSITION OF HYDROCELE FLUID

To the Editor:—*Have any studies been made on the enzymatic activity (lipase, esterase, acetyl choline esterase, and blood amylase) of hydrocele fluid? Not infrequently, one sees calcific plaques in the hydrocele sac containing large amounts of cholesterol. Have any determinations of the cholesterol content of hydrocele fluid been made?* *Ralph R. Landes, M.D., Danville, Va.*

Answer.—Hydrocele fluid in infants and children is derived from the peritoneal cavity through a hernial sac. In adults, particularly in elderly men, such fluid may represent an exudate from neighboring structures and possibly be associated with some inflammatory processes. This may also be the case with encysted hydroceles in the neck of the scrotum along the route of the original peritoneal evagination. Available information on the chemical constituents of peritoneal fluid is adequate except for the possible presence of enzymes. Both peritoneal fluid and transudates contain about 95% water. Traces of other constituents usually are expressed in milligrams per 100 cc. of fluid. The average cholesterol content of transudates is lower (40 mg. per 100 cc.) than that of peritoneal fluid (60 mg. per 100 cc.), but there is a wide range of variability. Both concentrations are much lower than that of cholesterol in plasma (195 to 230 mg. per 100 cc.). Peritoneal fluid shows lower average

concentrations in total nitrogen, albumin, and creatinine than do transudates. The pH of the two types of fluid is practically the same (7.4), as are the average content of chlorides, nonprotein nitrogen, urea nitrogen, and uric acid. Further details are given in the Handbook of Toxicology (edited by W. S. Spector, National Research Council, Philadelphia, W. B. Saunders Company, 1956).

OSCILLOSCOPE RADIATIONS

To the Editor:—*A patient has chronic erythema and edema of his eyelids and across the bridge of his nose. The findings are those of a contact dermatitis. The history reveals the use of an oscilloscope screen (5BP1-zinc orthosilicate) for observing electrical wave forms. The patient has spent as long as five hours at a time working with this instrument at a distance of about 14 in., although he states he averages only about one hour a week. Could this be the cause of his trouble?*

Edwin R. Ruskin, M.D., New Rochelle, N. Y.

Answer.—Although this query is lacking in much needed information, such as the wearing of spectacles, it is possible to state that any oscilloscope operating in good condition provides less threat of injury than equal exposure to a television screen. While some ultraviolet rays are generated, these are completely absorbed by the covering glass of the oscilloscope. The x-ray radiation is trivial in amount and soft in quality. Even at high relative acceleration potential the prospect of injury is less than that from the television screen. In the United States there are hundreds of scientists who for years, day in and out, have observed the oscilloscope screen without any record of injury at any time. It is stated that the observation distance is only 14 in. This, if true, might be conducive to more eye strain than in the case of a greater observation distance. Even so, eye strain would not account for the reported damage to the nose. Therefore, the condition described can have no connection to the power entering the oscilloscope or to any emanation therefrom.

CHRONIC ATROPHIC POLYCHONDRITIS

To the Editor:—*Is there a disease which has as one of its principal characteristics softening of the cartilages in the trachea and bronchi? This question concerns a patient whose larger bronchi and trachea tend to collapse on forceful inspiration and who is troubled with atelectasis.*

M.D., Minnesota.

Answer.—A rare disease, chronic atrophic polychondritis, is characterized by inflammatory destruction, degeneration, and fibrous replacement of cartilage throughout the body. It is likely to be prominent in the ears and in the cartilaginous portion of the nose. Some or all of the joints may be involved, as well as the costal cartilages, the larynx, and the entire tracheobronchial tree. The condition is often preceded by or associated with iritis or iridocyclitis. No infecting organisms have been found. Some patients respond well to treatment with steroids. While such a condition might be confined to the trachea and the large bronchi, such a case has not been reported. The nature of this condition is unknown, but it has been suggested that it is a peculiar form of allergic reaction. Chronic pulmonary disease with atelectasis, infection, and respiratory insufficiency has been the cause of death in the fatal cases.

RADIO TRANSMISSION THROUGH FILLINGS

To the Editor:—*A 32-year-old woman who has many silver fillings in her teeth, who is otherwise physically in good health, and whose only diagnosable disease is a chronic anxiety state claims that for many years she has been able to hear radio programs even when the radio is not turned on. This occurs from time to time, and if she turns on the local station she finds that what she has been hearing in her ears is the same program that is currently playing. She lives with her husband on a farm, and there is no neighbor's radio nearby. It has been said that occasionally silver fillings can do this sort of thing. Is this legend or fact?*

M.D., Ohio.

Answer.—When certain metals and their oxides are in a strong signal field of a radio transmitter, rectification may occur with the reception of the signal without the usual receiving equipment. This has occurred from radiators, faucets, and electric stove heating units but never from amalgam restorations or fillings. It is assumed that the farm on which the patient lives is not near a powerful radio transmitter. If so, a more intensive study of this unusual complaint should be made to determine whether other members of the household hear these radio programs. If the programs are heard only by the patient, the diagnosis and treatment are obvious. In view of the known anxiety state of the patient, the chief complaint should be evaluated more critically.

TREATMENT OF POISONOUS SNAKE BITES

To the Editor:—*The comments on treatment of poisonous snake bite, which appeared in the Questions and Answers section of* The Journal, *Jan. 3, 1959, pages 164-165, give the impression of being the latest information with which all are in agreement. This is not true, however, and the reader should realize that they represent Mrs. Buckley's personal feelings. It is unfor-*

tunate that this has resulted in the manufacturer's deleting reference to incision and suction in the circular accompanying their antivenin. Much work has been done regarding the effects of snake venom on animals. This has led to various conclusions, many of which do not apply to man. Due to the very nature of the problem, there are no well-controlled series evaluating the various therapies. There is little doubt, however, that the emphasis is shifting from incision, suction, and application of the tourniquet to more liberal use of antivenin, but this does not mean that the older techniques are without value if sensibly applied. The use of an arterial occlusive tourniquet is contraindicated, but the use of a tourniquet to block lymphatics is indicated. Much of the venom is transported via the superficial lymphatics, and the envenomation does not become systemic until these communicate with the deep lymphatics at the axilla, popliteal area, thigh, or groin. These superficial lymphatics can be blocked with a tourniquet loose enough to permit adequate arterial and venous circulation. Incising fang marks only compounds local damage from the venom, but incising the advancing edema front plus suction does remove a significant amount of venom. This was demonstrated by Jackson 30 years ago (South. M. J. **22**:605, 1929). *One must be careful in evaluating the results of therapy because of the many variables in a snake bite. Mrs. Buckley's suggested treatment would be adequate for most copperhead bites but would be inadequate for the bite of a large Florida or western diamondback rattlesnake. Many copperhead bites may need only antivenin, but a serious rattler bite will need incision, suction, tourniquet, adequate antivenin, and vigorous supportive measures, such as administration of blood, oxygen, and corticosteroids.*

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To the Editor:—*My letter in* The Journal *of Jan. 3, 1959, on the subject of snake envenomation, is not merely an expression of personl opinion but a compilation of medical opinion, published and in process of publication, on which the new, officially approved direction circular is based. Nowhere have I stated that "all are in agreement." The direction circular states, "Use of a tourniquet, incision and suction was for centuries the only method available for management of envenomation; such measures are still used by some physicians. However, others are coming to the opinion that surgical intervention should not be necessary if serotherapy is adequate." Much work has been done with the effects of snake venom in animals. Contrasting the results of Dudley Jackson, all Parrish's envenomated dogs, that were treated with incision and suction only, died. Although lymphatic spread of the venom received in the bite does take place, according to published reports, it is now believed that this is not the whole story. Parrish, whose work is summarized in the direction circular, stated that if any significant amount of venom is to be removed locally, early rather wide excision is required. Miller pointed out that this would be impossible on the foot, ankle, anterior surface of the leg, hands, and forearms. Parrish also emphasizes that "wide excision of any suitable body area would, of course, entail subsequent plastic surgery."*

The armed services were concerned with the question of the most satisfactory method for treatment of envenomation, because of snakebite accidents to military personnel. The studies of Leopold and co-workers and the observations of other authorities culminated in the request by the armed services for a new antivenin package from which the suction device is eliminated. This new package has been developed and has been officially standardized for military use.

The recommendations for dosage as given in the new direction circular reflect the experience of a number of clinicians practicing in snake-infested areas, as follows:

"INITIAL DOSE. It is essential to inject a large enough initial dose to overwhelm the poison. The smaller the body of the patient, the larger the initial dose required. Because children have less resistance and less body fluid with which to dilute the poison, they may require twice the dosage of serum that suffices for adults.

"Inject the contents of 1 to 5 vials of Antivenin or more, depending on the size of the snake, the lapse of time between the bite and specific treatment, and the size and condition of the patient (severity and rapidity of development of symptoms). For bites by large rattlesnakes and large specimens of other crotaline species, especially the tropical varieties, at least 5 vials of Antivenin or more may be required. Seven to 10 vials have been administered as the initial dose in many cases. For adult patients, as those weighing 100 to 150 pounds or more, 1 vial may be sufficient to neutralize the venom from the less virulent species, especially those of moderate size; e. g., copperheads or pygmy rattlers. For a bite by a similar specimen in a 20 to 40 pound patient, 3 to 5 vials may be required. Envenomation by a large cottonmouth moccasin may necessitate use of as large an initial dose as that for bites by rattlesnakes.

"ADMINISTRATION. If the bite was inflicted on an extremity, inject part of the initial dose intramuscularly (into muscle) or subcutaneously (under the skin) at various points around the limb, above the level of the swelling. Inject the rest of the initial dose into a large muscle higher on the bitten limb (the outer side of the thigh, the buttock or upper arm). Do not inject the serum into a finger or toe" (Shannon).

"If the bite was inflicted on the head or trunk, inject the initial dose subcutaneously or intramuscularly about the edges of the swelling surrounding the wound. Antivenin also may be injected subcutaneously in the loose tissue of the abdominal wall or between the shoulder blades. If a large amount of venom has been introduced directly into a superficial vein, as in a bite on the face, it may be desirable to inject Antivenin intramuscularly or intravenously within a few minutes. For late-treated patients exhibiting systemic symptoms, and especially in grave cases, associated with coma or paralysis, large doses should be administered intravenously."

The reported experience of Ruggiero showed that adequate antivenin treatment was effective in a severe case of Crotalus horridus (timber rattler) envenomation. Under local measures the patient's condition deteriorated rapidly, and he was moribund when antivenin was administered but recovered rapidly when mechanical measures were discontinued and adequate serotherapy was applied.

Supportive measures are described in the direction circular, in part, as follows: "The patient's blood should be typed as early as possible, since hemolysins present in the venom soon alter protein structure, thus preventing accurate crossmatching" (Shannon). "ACTH and cortisone may be used as a supplement to specific treatment, to control urticaria and similar delayed manifestations of allergy to horse serum, antibiotics and the venom itself. Such agents, however, do not of themselves influence the outcome of snake poisoning" (Wood, Hoback, Green; Schöttler). "Doses of 25 mg. cortisone have been administered by mouth, beginning with the first injection of serum, and continuing every six hours until all symptoms of envenomation were under control and no further doses of serum were required." According to one observer (Hoback) "such treatment has aided in reducing morbidity and has prevented evidences of serum sensitivity, even in known serum-sensitive patients. In severe cases cortisone may be administered intramuscularly or by vein if necessary."

Laboratory and clinical evidence has shown that the new, improved antivenin, released in March, 1954, does neutralize the proteolytic enzymes as well as the other toxic factors present in crotaline venoms. It is quite true that neutralization of the venom with antivenin is the only measure (officially) recommended. Infiltration of antivenin around the site of the bite is not advised in the newly revised direction circular.

According to properly constituted authority, cryotherapy is interdicted as a form of treatment. The new, approved direction circular states that this method, "first advocated for envenomation by Crum in 1906, has no therapeutic value" (Shannon, Parrish, Wood, and numerous others) "and is to be avoided as a form of treatment." "Combination of ligature and crymotherapy was tried and discarded (Allen) because such measures failed to save the lives of experimentally envenomated animals" (Allen). "Chilling, by chemical or other means, produces no alteration in the toxicity of the venom," (Shannon, Wood). "Prolonged exposure to cold is liable to increase the damage (Shannon). Since cold arrests conduction in the sensory nerves, however, ice water has been applied temporarily, by compress, in an effort to reduce the pain until serum could be administered. After injection of an adequate initial dose of Antivenin, application of cold is unwarranted and should be discontinued."

I shall be happy to send copies of the new direction circular on request.

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BACTERIOPHAGE TREATMENT OF STAPHYLOCOCCIC INFECTIONS

To the Editor:—*In the Nov. 8, 1958, issue of* The Journal, *page 1423, is a question on bacteriophage treatment of localized or systemic staphylococcic infections. The answer states that "today there is no practical method of employing bacteriophage therapy in the treatment of staphylococcic infections." This statement requires additional elucidation. The therapy is little used and little understood, but it probably represents the approach of the future. In the Communicable Disease Section of the Los Angeles County General Hospital, cures of staphylococcic meningitis and overwhelming septicemia have been effected with freshly made preparations lysing the patients' organisms. The preparations were given intravenously in both cases as well as intrathecally in the case of meningitis.*

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To the Editor:—*In the Question and Answer Section of* The Journal, *Nov. 8, 1958, page 1423, the consultant says that the great hope that bacteriophages would serve as effective thera-*

peutic agents against staphylococcic infections has never been realized. However, there is evidence that, when Staphylococcus bacteriophages prepared specifically for therapeutic purposes are used, they are of value. Practically all Staphylococcus bacteriophages have little, if any, effectiveness in vivo because they are inactivated rapidly in the presence of whole blood, serum, and pus. Such bacteriophages usually are prepared against a single strain or a pool of staphylococci in nutrient broth or peptone-free broth, and in these highly artificial conditions they do possess demonstrable and consistent lytic power. In my experience, however, such bacteriophages are useless as therapeutic agents.

Staphylococcus bacteriophages that act effectively in whole blood, serum, and pus can be prepared. For therapeutic purposes only those bacteriophages should be used that are virulent for the offending strain of Staphylococcus in the presence of the specific patient's whole blood, serum, or purulent exudate. It is also important that the bacteriophage to be used therapeutically can bring about lysis or convert the strain from smooth to rough at a temperature similar to that of the patient from whom the organism was isolated. Staphylococcus bacteriophages that have these attributes and are administered correctly can be useful in the treatment of local or systemic staphylococcic infections.

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To the Editor:—*In* The Journal, *Nov. 8, 1958, page 1423, the reply about the presently accepted opinion of bacteriophage treatment of localized or systemic staphylococcic infections states that today there is no practical method of using bacteriophage therapy in such conditions. On April 1, 1958, the Lincoln Foundation, a nonprofit medical research organization with laboratories in Swarthmore, Pa., was granted U. S. Government License 299 for Bacterial Antigen–Staphylococcus Phage Lysates (Staphage Lysates-T. M.). New biological products today must pass rigid criteria and strict evaluations with evidence of the need and merits and safety before such license is issued. Administered by nasal aerosol, orally, and topically, Staphage Lysates provide a practical method of controlling staphylococcic infections which concentrates on an immunological and lytic approach to this increasingly serious problem. This supervaccine with highly polyvalent phage activity enhances the natural, active defensive mechanisms of the host by lysing pathogenic staphylococci in their main habitat, the anterior nares. Staphage Lysates selectively kill Staphylococcus pyogenes var. aureus yet spare the useful saprophytes of the intestinal flora, so essential in the bacterial synthesis of vitamins. The lysates contain bacterial polysaccharides which have been shown to be a potent agent for stimulation of higher levels of serum properdin, providing a nonspecific immunity against invasion by all bacteria and viruses. Many of the older articles on bacteriophagy stressed the value of specific staphylococcic phages in the treatment of staphylococcic infections (Crutchfield and Stout,* Arch. Dermat. & Syph. **22**:*1010, 1930).*

I have contacted most of the competent authorities in the investigative field dealing with antibiotics. Laboratory studies with clinical evaluations are being conducted on many fronts, the results of which will be published soon. The emergence of resistant strains of Staph. pyogenes var. aureus shows that the probable answer to this perplexing problem may not lie in the development of more new antibiotics, or combinations of them, but in the host, his environment, and his protective mechanisms. Being a nonprofit group, the trustees of the Lincoln Foundation have not applied for a patent on their product, but they do wish to disseminate the more recent knowledge of staphylococcic phages gained in the past 12 years of intensive work with Staphage Lysates. We have profited immensely from the background of mistakes and truths obtained during the 1920's and 1930's when bacteriophage was in its heyday. These facts warrant a critical reappraisal of staphylococcic bacteriophagology in the fight to overcome the serologic supremacy of the pathogenic micrococci, especially since resistance to phagic lysis has not been observed and the "hot" epidemic, hospital strains of Staph. pyogenes var. aureus—phage pattern 80/81—are readily lysed by Staphage Lysates.

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MUSCLE CRAMPS

To the Editor:—*In* The Journal, *Dec. 20, 1958, page 2206, a question was asked relative to the treatment of muscle cramps. Years ago, a patient began having cramps in the legs at night and a colleague suggested the use of quinine sulfate, which he had given for years, with success. Since then, from personal experience and in patients, regardless of any rationale, it has worked, which seems to be sufficient justification for its use. One 0.3-Gm. capsule has usually been sufficient to ward off the attacks for weeks and often months. Failure has been extremely rare.*

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